

The Canadian Medical Association Journal

Vol. XVI

TORONTO, APRIL, 1926

No. 4

An Address

ON

NEPHROSIS*

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WITHIN recent years the term nephrosis has bulked largely in the literature of Bright's disease. The term is good in that it distinguishes what is essentially a degenerative condition from true inflammatory nephritis. But it has its dangers. Glomerulo-nephritis is a very definite clinical and pathological entity. In spite of the prominence which Volhard and Fahr give to it, nephrosis, on the other hand, is to be regarded rather as a group of states than as an entity. It is a degenerative condition affecting the epithelial cells of the convoluted tubules, and supposed to be associated with a train of clinical phenomena of sufficient constancy to entitle it to be regarded as a disease. For clear thinking it is vital to distinguish between, on the one hand, the degeneration of the tubular epithelium which is certainly a nephrosis or nephropathy, but which may owe its origin to a great variety of pathogenic factors, and on the other hand, the clinical complex which the term nephrosis connotes to Volhard and Fahr, Epstein, and others.

A nephrotic or degenerative condition of the tubules may be found in death from many acute infections, amongst which we may instance pneumonia, typhoid fever, and in particular, diphtheria. Chronic infections such as tuberculosis and syphilis, the inorganic poisons such as mercuric salts, chromates, and tartrates used to produce so-called experimental nephritis,

and organic poisons as in jaundice, diabetes, hæmoglobinuria, and the toxic kidney of pregnancy, may all give rise to pathological lesions in the kidney which we may rightly name nephrotic, but unaccompanied by the full clinical picture which justify us in diagnosing the disease nephrosis.

In addition to this catalogue of conditions which may or may not be called nephrosis, and which for the most part may be spoken of as the acute type, Volhard and Fahr describe a condition, admittedly rare, which they name "genuine nephrosis," of unknown etiology, and presenting a train of clinical phenomena, which make up a rather remarkable picture. The patient as a rule is young, and the principal changes are œdema, marked albuminuria, a urine with a high specific gravity and abundant casts but no red blood cells, low blood pressure, a moderate but progressive anæmia, marked salt retention, normal blood urea and total non-protein nitrogen, but decrease in the total blood proteins with inversion of the normal ratio of albumen to globulin (2 to 1), a great increase in the blood cholesterol, and a low basal metabolism. The three most striking features are the œdema, the albuminuria, and the hypercholesterolaemia which may reach as high as 800 mgm. per 100 c.c.

The question arises, have we any right to regard the condition as a true *renal* disease? In amyloid disease the connective tissue of the kidney manifests a degenerative change which is also found in other parts of the body, but

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we do not attribute the disease to the renal lesions. So in nephrosis it may well be that we are dealing with some primary disturbance of metabolism, particularly of cholesterol, in which the kidney merely plays a part, and not a leading one. In a characteristic case studied by Major and Helwig¹ the liver as well as the kidney showed marked deposits of lipid. One of the most typical cases of a nephrotic kidney which I have had the opportunity to study was in reality a case of thyroid and parathyroid insufficiency, in which tetany and a high blood cholesterol were two of the most striking clinical features. The details of this case, which is referred to below, have been published by Davidson².

The so-called kidney of pregnancy is another illustration of the same truth. It is not a renal disease, but a toxæsis with renal complications. It shows some of the features both of nephrosis and nephritis. The albuminuria may be associated with red blood cells in the urine. Other symptoms are œdema, high blood pressure, convulsions, and retinal disturbance. The blood urea is normal, and the functional renal tests show no abnormality apart from chloride retention. The most interesting feature of the condition is that the albuminuria and casts may disappear within six hours after delivery, with great diminution of the œdema in the same length of time.

Morbid anatomy.—The kidney is large and pale. Here, therefore, we have an example of the large white kidney, indistinguishable to the naked eye from the large white kidney of the second stage of glomerulo-nephritis, but presenting an absolutely different picture under the microscope. The cause of the swelling and pallor is the same, the accumulation of lipid droplets in the cells of the parenchyma. On section the cortex is swollen and pale, and yellow spots or streaks are often discernible.

In rare cases the organ may present the peculiar appearance known as the "myelin kidney". The term is of the same order as the "large white kidney", and indicates a naked eye picture of great deposits of a myelin or lipid substance. It is not peculiar to the nephrotic kidney, but is also found in the second stage (large white kidney) of glomerulo-nephritis. In a typical case the inner half of the cortex is occupied by a bright yellowish zone which sends

streaks up into the cortex. The condition was fully investigated by Löhlein³ in 1905, and important new points were brought out by Munk⁴ in 1913. McNee⁵ gives an excellent resumé of the condition with a description of three cases together with a good picture of the gross appearance. Only one example occurred in our own material, a very peculiar case of thyroid and parathyroid insufficiency associated with tetany in a girl eighteen years of age, who presented a typical clinical picture of nephrosis with great œdema and a very high blood cholesterol, together with remarkable lipid deposits in the cells of the convoluted tubules and a characteristic "myelin kidney" in the gross.

Microscopic examination shows the condition to be essentially a tubular degeneration with no sign of inflammation, so that the term tubular nephritis commonly applied to it is an undesirable one. The epithelium of the convoluted tubules is profoundly degenerated, and is seen to contain great numbers of droplets. These droplets take on the Scharlach R. stain, and many of them consist of the neutral fat seen in ordinary fatty degeneration of the kidney. In addition, however, we find numerous droplets which appear in frozen sections as bright, doubly refractive bodies under crossed Nicol's prisms, and are therefore not to be regarded as neutral fats but as lipid or fat-like in nature, bodies which, occurring in the normal adrenal cortex, Virchow originally called myelin. They consist of an ester of cholesterol. It is this lipid which, when present in sufficiently large amount, gives rise to the gross picture of the myelin kidney. As the result of his studies Munk came to the conclusion that the lipid appears as the result of damage severe enough to cause complete destruction of the cell, whereas the neutral fats were associated with a less extreme degree of injury. A very remarkable feature is to be observed in the distribution of the lipid, for not only is it found within the epithelial cells of the tubules, but also in the interstitial tissue either enclosed in phagocytic endothelial cells to which it gives a "foamy" appearance or lying free as the result, probably, of the disintegration of these cells. Munk found the lipid in abundance in kidneys which he regarded as syphilitic, and in these cases the urinary casts contained similar material.

The glomeruli in a pure case show no ap-

parent alteration. That they do not escape unscathed, however, is suggested by the presence of albumen in the capsular space, which can be coagulated by heat and thus demonstrated to best advantage. The significance of this observation will be referred to presently.

Relation of symptoms to lesions.—It is peculiarly difficult, indeed impossible, to explain the symptoms of nephrosis by the anatomical changes present in the kidney. Oedema with chloride retention and albuminuria are phenomena which on theoretical grounds should be associated with the glomeruli, and yet they are the dominant features of this condition in which the lesion is apparently a tubular one. The paradox can only be explained away by a series of guesses. The mystery of oedema is still unsolved; we really understand very little of the essential mechanism by virtue of which fluid collects in the tissues and in the serous sacs. It may be that the cause of the oedema of nephrosis lies in the kidney, but it is even more probable that it should be sought elsewhere, for the toxin which acts on the kidneys must at the same time act upon the blood vessels and upon the tissues in general. Something causes the water of the blood to pass into the tissues instead of into the urine. Retention of chlorides in the tissues will naturally hold the water back, but as the chlorides are excreted by the glomeruli it is difficult to see why they should be retained as the result of a lesion which is essentially tubular. It may be, as Cushny has suggested, that the delicate filtering membrane of the glomerulus may be damaged without presenting any anatomical evidence, and may thus allow the passage of large albuminous molecules which at the same time block the pores to the passage of the smaller salt molecules. Here, however, we are indulging in fanciful speculation out of place in the science of morbid anatomy.

Some of the albumen appears undoubtedly to be glomerular in origin, as it can be demonstrated in the capsular space. Much of it probably also comes from the degenerating and disintegrating tubular epithelium. The casts which are so abundant in the urinary deposit probably owe their origin in the same way both to the glomeruli and to the tubules.

One of the most characteristic features of true nephrosis is the high blood cholesterol and the presence in the urine of fatty globules,

which under the polarizing microscope are seen to be doubly refracting, and to present the bright Maltese cross of light so characteristic of cholesterol ester. These findings must be associated with the great accumulation of cholesterol esters in the epithelium of the convoluted tubules. Of the meaning of these peculiar phenomena we are completely in the dark. It would appear, as suggested above, that perhaps the essential basis of nephrosis is some fundamental disturbance of cholesterol metabolism, a subject of which we know at present next to nothing.

The normal blood urea would suggest that the renal filter in the glomeruli must be performing its function properly. The normal blood pressure is due to the fact that there is no obstruction to the blood flow through the glomeruli, so that there is no call for a heightened pressure to enable the remaining glomeruli to keep the blood metabolites at a normal level.

We may conclude this discussion on nephrosis by paradoxically asking the question: is there really such a condition? It is like eczema in skin diseases: the more carefully a case is studied the more reluctant is one to rest content with a diagnosis of nephrosis. The case of thyroid and parathyroid insufficiency has already been cited. It is true that this patient presented oedema, albuminuria, and hypercholesterolaemia, but we regarded her as suffering from a general metabolic disturbance rather than a local renal one.

A true nephrosis has no right to develop glomerular symptoms: if it does so the diagnosis must be reconsidered. Of these glomerular symptoms the principal are hypertension, retention of non-protein nitrogen, and a low fixed specific gravity of the urine. But what are we to say of the following case? A young girl, fifteen years of age, developed without apparent cause marked oedema of the face and legs. The urine contained a large amount of albumen and a few hyaline casts, with a specific gravity of 1030. The blood pressure was 112. Urea was excreted in the urine to the amount of 3 per cent, and there was no urea retention in the blood. The blood cholesterol was 393 mgms. per 100 c.c., and there was marked chloride retention. A typical picture of nephrosis. Three years later the oedema had disappeared, the specific gravity of the urine was low and fixed, the blood urea was high, and uraemia with ama-

rosis developed which proved fatal, an end picture equally typical of glomerulo-nephritis.

Kaufmann and Mason⁶ are of the opinion that a nephrotic kidney may progress into a secondary contracted type, to be distinguished from the primary contracted kidney of glomerulo-nephritis. They describe a carefully studied case in which the patient passed through a first stage of the typical nephrotic type, and then entered upon a second stage in which such features as hypertension, retinal changes, and nitrogen retention were superadded. Whether such cases and the one recounted above should be regarded as nephrosis progressing to renal insufficiency or as true but atypical glomerulo-

nephritis from the beginning is open to question, a question which must still remain unanswered.

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COMPLEMENT IN HEALTH AND IN DISEASE

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HOWEVER complicated immunity problems may be they always furnish interesting subjects for investigation. Also, this wide field happily supplies a mental playground for medical men, for surely no physician is so bound to the routine of his daily work, or so involved in the subtle scientific intricacies of modern medical practice that he neglects to let his thoughts dwell on the broader aspects—the unexplained marvels of immunity phenomena—that come under his daily observation.

The difficulty experienced in discussing a problem in immunity is to confine ourselves to that single problem. The opinions and experiments concerned with each point of view or theory are numerous, complicated and technical. A study of a single factor with all its associated biological phenomena, involves us in a consideration of other problems in the wide question of infection and resistance.

Phagocytosis, the antibacterial action of the body fluids, the bacteriophage, the mechanical and chemical protection provided by certain cells, afford varied factors in the body's resistance to infection; but for the purpose of this discussion we will attempt to limit ourselves to a consideration of a phase of the bactericidal

property of the blood serum—namely, the foreign body—antibody—complement reaction.

The response to the invasion of the body tissues by a foreign agent is observed in the formation of an antibody. The action of the antibody on the foreign body is facilitated in some, if not all, instances, by a third substance—complement or alexin. The fluctuation in the power of the latter factor has been the subject of but limited investigation.

This complement may be defined as a substance of unknown nature, present in the blood serum, by means of which the latter is able to take part in certain immunological reactions. Complement is thermolabile in the sense that it is rapidly destroyed at 55° C., and it is, moreover, extremely sensitive to the action of acids and alkalis. Normally, after removal of the blood from the body this immunological power gradually disappears; also, it may be destroyed by shaking; and finally, under certain conditions, it may be reactivated.

Although the nature of this substance is indefinite, yet a fairly accurate estimation of its ability to take part in certain immunological reactions may be demonstrated by the use of the complement fixation test. As is well known,

this test is one of the most striking phenomena concerned in the problem of immunity. It involves and depends upon the interaction of the foreign body (infective agent), the antibody (amboceptor) and the complement (alexin). The practical and valuable application of the principles of variation among these three substances, as may be determined in vitro, is exemplified in the serum test for syphilis and other diseases.

The variations in the three factors, foreign body, antibody and complement within the tissues, and the endless variations in relation to one another give rise largely to the difference in symptoms and results observed in many infectious diseases. The nature of the foreign body may be considered accidental, but the formation and the use of the antibody depend on the body tissues.

With this in mind it was thought that a further study of the variations in the power of the complement in health and in disease would prove of advantage. Investigations were carried out on the blood of 230 normal persons and 280 patients suffering from various diseases. The persons in normal health included children, students, laboratory workers and prisoners. A specimen of blood from a prisoner represented a portion of that which it was necessary to obtain for the routine Wassermann examination. The regular life and diet of the prisoners naturally was conducive to a uniform standard of health.

Technique.—The blood was collected from a vein into a sterile vacuum tube. All specimens were collected at the same hour of the morning in order to obviate, as far as possible, any variations in the complement content that might arise following the ingestion of food. The specimens were placed in the incubator for thirty minutes and were then removed to the icebox where they were left for four hours before the tests were carried out. They were not centrifuged, as centrifuging was found to cause variations in complement content. Some specimens were left in the icebox for twenty-six hours. Variations in the complement titre between those left in the icebox for four hours and those left for twenty-six hours were found to be negligible.

One-half c.c. of each individual serum was withdrawn from its container and sufficient normal saline added to make a dilution of one

in fifty. A series of test tubes was set up for each specimen, and to those were added the same amount of sensitized sheep cell mixture, and sufficient saline to make an equal total volume.

Amboceptor for sheep cells of the same titre was used throughout all the tests. Specimens containing an excess of natural sheep cell amboceptor were discarded.

TABLE 1

Test tubes	75mm. 9mm. No. 1	2	3	4	5	6	7	8	9	10
in c.c.	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Sensitized cells	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Normal saline ...	0.9	0.8	0.7	0.6	0.5	0.4	0.3	0.2	0.1	0

The tubes were incubated for thirty minutes, then removed from the incubator and allowed to stand for one hour at room temperature; readings were then taken. A second method was to place the tubes in the icebox for eighteen hours before the readings were made. No appreciable difference was noted between the results obtained by the two different methods.

The tube containing the least amount of diluted serum which showed complete hæmolysis was taken as the titre of the complement power for that particular specimen. If no hæmolysis was noted in tube 10 the strength of the original serum dilutions was doubled and another series of tests set up. In four instances the use of undiluted serum failed to produce hæmolysis.

Findings in Health.—The reactions on the specimens of blood taken from persons in normal health gave a fairly uniform result. In 224 cases out of 230 examined with the technique adopted, complete hæmolysis took place between tubes 5 to 8.

Variations from these findings were noted in six cases. In these twice the normal amount of serum was required to produce hæmolysis. Investigations showed that one of these persons was recovering from influenza, one from diphtheria, while two proved to have nephritis and one developed into a definite case of endocarditis. The serum from one person who had no definite demonstrable pathological condition though he was of a sallow type and complained of fatigue on exertion, gave a complement titre of but 65 per cent normal.

Investigations were made on the blood of three persons in normal health to determine whether there was any variation depending

on the time of day the specimen was taken, or if there existed a variation in relation to meals. If, in the titration of such blood, hæmolysis took place in tube 6 in the morning specimen the rule was for the complement power to be increased by evening when complete hæmolysis might be noted in tube 5. There was never more than a one tube variation. However, the complement power of these persons frequently showed a weekly difference as wide as that found between persons in normal health; that is, while the blood of such a person gave complete hæmolysis in tube 5 one day, it might not give complete hæmolysis up to tube 8 a week later, or vice versa. The age of a person apparently made no appreciable difference in the complement power of the blood serum; the average age of those in normal health was twenty-five years.

Findings in Disease.—There seems to be no absolute rule for the variations found in the complement of patients' blood during disease. However, the investigations carried out on 280 patients indicated the existence of a fairly uniform reaction throughout the course of an acute infection. Commonly there was a slight increase of complement at the onset of the symptoms of disease, followed by a steady decline as the symptoms subsided, and during convalescence the complement gradually returned to normal. Similarly too, there was an increase of complement coincident with the onset of complications. Many fatal cases, however, showed a steady decrease in complement, and in some no reaction indicating its presence could be obtained.

While throughout the course of an illness fluctuations in the amount of complement may follow a general rule, the investigations of the substance in certain diseases showed that there was a wide and striking variation depending on the nature and location of the infection. In septicæmia, endocarditis and nephritis the decrease was, as a rule, distinct, while in syphilis, chronic tuberculosis and chronic arthritis the loss was slight. Serum from patients with uncomplicated malignant disease, pernicious anæmia, goitre and diabetes gave but a slight change in alexin content.

The investigations of sixteen cases of septicæmia showed that there was a loss of complement ranging from half normal to total absence. Twelve of these cases proved fatal. Specimens

of blood from twenty-one patients with diseased hearts were examined. Valvular lesions, without evidence of existing infection, gave results which were normal, or close to normal; on the other hand, in eight cases diagnosed as subacute bacterial endocarditis a decided decrease in complement was noted progressive with the course of the disease, and in each fatal case there occurred, eventually, a decrease of from 50 to 100 per cent. Three cases diagnosed as bacterial endocarditis gave a normal complement titre, these three patients recovered. In none of the three was a positive blood culture ever obtained. A complement titre of half normal was found in two cases of auricular fibrillation, and in one case of myocarditis following diphtheria.

A loss of complement of 50 per cent or more was also noted in some cases of pneumonia, peritonitis, cellulitis, acute rheumatism and other severe infections. On the other hand, many cases were examined in which there was the usual slight variation in complement during the course of the disease, but which showed no evidence of a progressive decrease. Also, in five cases of severe illness the blood gave a normal complement titre even when taken a few hours before a fatal termination to such an illness. This is in agreement with a finding of Gunn¹ in his comprehensive study of the variations of complement in diphtheria, scarlet fever and typhoid.

As a rule there was noted a decrease of complement in cases of nephritis. The decrease varied from 5 per cent below normal to complete absence. This refers to cases of nephritis of unknown origin and also to those following infectious diseases. In acute nephritis the complement rapidly returned to normal on subsidence of the symptoms, but in chronic nephritis it remained deficient, eventually becoming almost or entirely absent in those cases that progressed to a fatal termination. Rockwood and Beeler², however, noted that patients with severe uræmia showed no significant variation in the complement content of the serum.

It was thought that it would prove of interest to investigate the complement power of patients' blood before and after transfusions of small amounts of blood serum. Examinations were made on five such patients who were known to be deficient in complement, and in three the increase in this substance after transfusion

varied from 10 to 40 per cent. There was no response in two patients who were in a moribund condition from septicemia. An increase of 40 per cent was obtained in one case by the transfusion of but 20 c.c. of fresh serum. This latter patient, severely ill with a streptococcus hemolyticus septicemia and with almost entire loss of complement, was treated with repeated transfusions of fresh human serum, together with inoculations of rabbit serum containing an amboceptor which had been prepared by the use of the specific streptococcus. There was a striking beneficial response to the treatment and the patient recovered.

Two specimens of blood out of 510 examined were found to be anticomplementary when tested against guinea pig complement. One of these serums was obtained from a patient suffering from a bacterial endocarditis, and one from a patient with a severe nephritis with uremic symptoms. High dilutions of these serums did not bring about hemolysis, and microscopic examination of the sediment showed that the cells were not destroyed.

Attempts were made, *in vitro*, to reactivate the complement in four serums from patients when these serums had shown almost a complete absence of complement power. Reactivation, showing an increase of alexin over that of the original specimen, and varying from 10 to 30 per cent was obtained by the addition of fresh serum in three instances.

Discussion.—The findings for normal persons indicate that in health the complement content of the blood is fairly constant. Any decrease of more than 25 per cent under the normal suggests a careful scrutiny of that person's condition. I think it justifiable to consider a high complement power as a beneficial factor in immunity.

While the complement titre of the blood shows, as a rule, definite fluctuations at certain periods in the course of a disease that is due to infection, and also wide variations depending on the severity, character and location of the infection, yet there are exceptions which make it impossible to draw absolute conclusions. *A slight fall of complement that coincides with an improvement in the patient's condition indicates that immune bodies are being formed with a subsequent binding of complement. Such a variation in complement was noted in pa-*

tients in whom there was a favourable outcome. However, the decided and progressive loss of this substance, more especially during those diseases that terminate fatally, would suggest that the finding of a persistent low complement power in disease is to be considered of grave significance, and the finding of a steady and progressive loss of this power is a bad prognostic sign. Such an extreme loss was occasionally noted in patients who were apparently doing well, but who afterwards did badly. In such cases, and the findings most frequently occurred in endocarditis, the investigations may prove of value as an aid to diagnosis. Finally, since complement is so much concerned in body immunity, it would seem justifiable, when so required, to treat the patient with a view to either stimulating the production of, or to replacing this substance.

The question arises: Is alexin essential to life? Two cases of disease in which a complete absence extending over months was noted, proved fatal. Yet one of the normal cases investigated—a girl who had recovered from an attack of diphtheria—showed almost complete absence of complement for months, and still the girl appeared to be in good health. Also, two patients with chronic nephritis and one with endocarditis showed a severe loss of complement extending over a period of three years, and, while the outcome was fatal, during that time these patients gave no evidence of disease other than would be expected from the essential condition. One apparently normal case showed a diminution of complement power of over 25 per cent.

In this connection it is well to note that there has been discovered a race of guinea pigs in the blood of which active alexin was found to be greatly diminished.⁸ They were reported, however, to lack the vitality of the average stock. Apparently, then, life itself is possible in the absence or decrease of complement as may be determined by the examination of the blood serum.

Now, the reason for the diminution of complement in disease is not established. Is there a failure of the tissues to produce it? Is it bound in the body-antibody reaction, or is it destroyed or inactivated? These are questions that have been the subject of extensive investigation and to decide which will require considerably more experimental evidence than is at present avail-

able. Evidently, during the course of a disease, there is some relation between antibody content of the blood, and complement. A slight diminution of complement is to be noted coincident with the formation of immune bodies, otherwise this relation is not definite. Evidently, too, the complement power does not vary directly with the blood cell count. In pernicious anaemia the average was nearly normal; moreover patients with a low red cell count frequently gave a high complement titre. Patients were also noted who, with a leucocyte count of 20,000 or more, showed an extreme loss of complement, while again, other patients with the same count showed an increase over normal in the alexin titre.

As for reactivation: in vitro, such reactivation as we could obtain by the addition of fresh serum to a serum of a patient which was deficient in complement averaged 20 per cent. In vivo, alexin may be reactivated, or its production is stimulated by the transfusion of even small amounts of serum high in complement power.

The source of complement is unknown. The frequent findings of a diminution in conditions affecting the heart and kidneys, as indicated in these studies, offers a problem for further investigation.

Therapeutic value of Complement.—The discussion of the therapeutic value of the complement calls for a study of the exceptions noted in these investigations, and again, to a consideration of the body-antibody-complement reaction. Occasionally it was observed that during the course of a severe illness, and even up to a fatal termination, the complement power of the patient's blood was practically normal. *If the complement power is high and the patient is not doing well, it is probable that the antibody content of the blood to the specific organism is low.* Such was found to be so in six cases of this character investigated in order to determine the antibody content of the blood. Also, this offers one explanation for the chronic character of certain diseases, even though a high complement power may be present; that is, sufficient antibodies may not exist in the blood to unite with the alexin in order to destroy the infective agent.

Conversely, it was noted that some patients with a definite infection had a high antibody content in the blood and a persistently low complement power. If the complement power were

raised would those patients improve, and what construction may be placed on such findings as to make them of value in the treatment of the case?

The resources of medicine are directed towards the elimination of the foreign body and towards aiding the development of resistance on the part of the patient. This resistance, as concerned with known infection, may be considered, in part, as due to the development of a specific antibody and to the formation and use of complement.

Scientific medicine has occasionally endeavoured to supply the antibody but what of the complement? Also, has sufficient consideration been given to the specific nature of the antibodies and their definite quantitative relation with the complement.

For instance, let us consider the case of anti-streptococcus serum, a float thrown without enthusiasm by the physician to the sinking patient with a streptococcus infection. Wherein does it lack its sustaining power? First, there are many strains of streptococci, and usually the serum is minus the specific antibody to the essential strain, a possibility that is generally recognized. Second, but not so generally recognized, if we are fortunate enough to obtain a serum containing a specific antibody, the patient may lack the complement necessary to make the specific reaction possible. The active complement in such stock streptococcic serums has long since disappeared.

It was noted before that in some cases, by means of transfusions or inoculations of even small amounts of fresh serum the complement titre of the patient's blood may be raised. Such a procedure would appear to be logical when indicated by the finding of a low complement power in the patient's blood. Again, if the complement power is high and the antibody content of the patient's blood is low, the natural indication is for the therapeutic use of specific antibodies. The use of such antibodies depends upon the determination of the infective agent and the preparation of a serum containing the specific antibody, at present our most difficult problem.

The method adopted for the therapeutic use of serum containing antibodies or complement is one for serious consideration. It would appear safer to give a serum containing only anti-

bodies, by the subcutaneous method. *Such a serum, containing powerful amboceptors, if given intravenously, may cause too sudden and too great a liberation of bacterial endotoxins.* Also, since complement is required to complete the reaction, it may make a sudden and severe demand on the complement reserves of the body. When a titration of a patient's serum indicates that the complement power is low, one should proceed cautiously in the use of a therapeutic agent that makes further demands on the exhausted complement reserves.

The relative value of the different methods, subcutaneous, intramuscular or intravenous, for the therapeutic use of serum containing complement, remains to be determined. The intravenous method, at present, appears the best although success has been obtained by the subcutaneous inoculation of fresh serum.

Transfusions of whole blood have been used frequently in the treatment of severe infections, and the giving of small repeated transfusions, as reported by Polak⁴ and others, appears to have been of value. The favourable results obtained have been considered to be either, because of an increase in the blood cells, or of a foreign body reaction, or of the action of the antibodies that were contained in the blood used for the transfusion. It is probable, however, that some of the fortunate, though unexplained, beneficial results occasionally obtained by such transfusions of blood in septic cases may have been due to the action of the complement. On the other hand, many observers are critical of the value to be derived from blood transfusions in septic cases. Baldwin⁵, in an extensive survey of the subject, comes to the conclusion that such transfusions are of no value in acute sepsis.

These opinions, for and against, are based on the study of the results obtained from the use of whole blood and a brief consideration of one essential factor is relative to this discussion on complement. There are two classes of cases for which transfusions have been used—those due to deficient cellular elements in the blood, and those due to deficient qualities in the serum. The latter condition is, as a rule, the result of infection. Now, if there are substances, already present in the blood, or added to the blood used in the transfusion, which act as a foreign body, then more strain is thrown on the complement reserve of the patient. Transfusions in a pa-

tient with deficient serum qualities might well fail of their purpose or even prove dangerous. This is of surgical interest, for the question of the necessity for a transfusion is often a surgical consideration, and a patient low in complement titre is naturally a poorer surgical risk than one with a normal or high complement power.

Experience has shown that any method of therapeutics which demands blood transfusions should be approached with reserve; there are well known risks connected with the procedure, and inherent dangers in the use of repeated transfusions.

For the intravenous use of complement one of these dangers—that of the patient's reaction to the donor's cells—may be eliminated by allowing the donor's blood to clot and using the serum alone. Moreover, but comparatively small amounts of serum, 30 c.c. or less, have been used with beneficial results.

It is important to note in this connection that human serum is low in complement power compared to that of some animals. Guinea pigs frequently show a complement power of the blood approximately six times as high as that of the human blood. We need not be limited to the use of human blood in order to supply this substance, provided, of course, we are able to use a serum high in complement power, that will not develop anticomplements or anaphylaxis.

In conclusion, I wish to point out that in drawing deductions from these findings one is on the uncertain ground of complicated immunity problems. Three of these problems are particularly concerned with this discussion. First: the power of the complement was estimated only by the hæmolytic method. However, it is known that the agglutinin and bactériolytic strength of this substance closely parallel the hæmolytic power. Second: there is the much disputed question of the multiplicity of complements—were we dealing with one or with several? It may be noted—whether one or several—the reactions were fairly uniform. Third: while it has been shown by Watanabe⁶ and others that complement exists in the blood serum in practically the same amount as in the corresponding blood plasma, yet we can but surmise as to the action and value of the complement in the circulating blood; the deductions were made from findings obtained by the in-

vestigation of blood serums, the theory being that there exists but little variation between the action of the complement found in the blood serum and that of the circulating blood.

I wish to express my appreciation to Dr. C. E. Corrigan for valuable assistance in carrying out the technical work.

Summary

Investigations were made in order to determine the strength of complement in the blood serum of 230 apparently normal persons, and of 280 patients suffering from various illnesses.

The findings indicate that high complement power is a beneficial factor in immunity. In

health the complement power of the blood serum varies within narrow limits, while in disease it may vary widely, depending on the nature, location and stage of the disease.

In some cases an estimation of this power is of value in diagnosis and prognosis, and furnishes an indication for a method of treatment.

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X-RAYS AND RADIUM IN THE MANAGEMENT OF BREAST CARCINOMA*

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IT HAS been the custom for a number of years past to make use of both x-rays and radium as adjuncts to surgery during some stage of the treatment of breast cancer. Some surgeons restrict this use to post-operative radiation by x-rays; a few only have used either x-rays or radium as a pre-operative procedure or preparation for a subsequent operation. Most surgeons will admit that there is some value in this radiation but there are a few who deny any virtue—indeed there are some others who believe the method detrimental.

This diversity of opinion would seem to indicate either that the procedure as carried out by some radiologists is ineffective, or that the type of cases referred by the surgeon is so unsuitable either in its stage of development or in some other important factor as to nullify the benefits possible from the treatment, and it is not remarkable that there should be considerable divergence of opinion, when we consider that the technique of radiation therapy has been

going through a period of such rapid development as has been the case during the past years. Much of this work has been entirely empirical, and cannot progress beyond this stage until we are in possession of much more accurate information than we now have as to the exact manner in which x-rays and radium produce the effects, which they undoubtedly do exert upon malignant cells.

The observations which form the starting point for most of our reasoning on this subject centre around the disappearance of superficial epitheliomata of the skin following the application of an erythema skin dose of either x-rays or radium. Such lesions are cured in well over 90 per cent of cases if a proper dose is administered. It was therefore assumed that if a similar dose could be applied to a carcinoma of the breast, a similar result would be obtained, and the great effort of the past ten years has been directed towards perfecting apparatus and a method by which this desired result might be obtained. It may now be said that this is technically quite possible, but hav-

* Read at the meeting of the Canadian Medical Association, Regina, June, 1925.

ing reached this point we find that the problem is much more complex than the mere physical problem of delivering to the cancer mass a certain measured amount of rays, either x-rays or radium and find the cancer disappear.

The great problem at present is to discover in what manner this effect is produced. At first sight it would appear that the rays directly killed the cancer cell, and this was the opinion held by the majority of workers until a comparatively short time ago. According to this idea cancer cells are more sensitive to radiation than normal tissue cells, and are destroyed by a dose of rays which does not cause any harmful effects in normal tissue: that is to say that a margin of considerable latitude exists between the response offered by these two types of cell and further that this margin varies with almost every individual type of malignant cell.

There is a great mass of evidence to support such a theory. Beginning with such cells as basal cell epithelioma or lympho-sarcoma, we find cells which are very easily influenced as a rule—in fact which frequently disappear almost as if by magic with comparatively small doses. As the epithelial cell approaches the squamous type however, it becomes more resistant and we find a squamous-cell epithelioma requiring several times the dosage which the basal cell lesion requires. When we progress to the cylindrical form of cell the margin of safety between the dose necessary to destroy the cancer, and that which will at the same time destroy the normal tissue has been reduced almost to the vanishing point. In such cases if x-rays or radium are used in the doses necessary to destroy the cancer extensive sloughing is likely to occur.

This reasoning has dominated most of the therapeutic application of both radium and x-rays for many years. As it has been applied to the treatment of breast carcinoma the statement has commonly been made that if during the operation a few cells remained which the surgeon could not remove, then the x-ray would destroy them and thus prolong or save the patient's life.

Recent experimental work however has shed more light upon this important subject and seems to indicate that some, if not most of the effects produced by x-rays are due not to the direct destructive action of the rays upon the cancer

cells but rather to an indirect effect induced in the normal body cells. It further appears that this is somewhat analogous to an immunity effect which renders the normal tissue almost impossible soil for the cancer to grow upon.

Some of these experiments are of sufficient general interest and have such immediate bearing upon our whole problem as to justify quoting from the original article. (Nakahara—*Exp. Med.*, July, 1923, xiii)

Sixteen mice, after etherization, were shaved in the upper abdomen and groins and so arranged as to expose the left groin to x-rays while the whole of the remainder of the body was protected.

To the exposed left groin a full erythema dose of x-rays was then administered and when the erythema was established cancer grafts were inoculated into the groin which had received the treatment and also into the groin which had received no treatment. Several of these mice were killed in pairs in order to study the effects as they progressed, but six were allowed to live three weeks. It was then found that five out of six of the inoculations in the protected area resulted in healthy tumours, *whereas only one tumour developed out of the six inoculations made in the areas which had received x-ray treatment.*

It should not be necessary to emphasize the point that this experiment therefore is a purely prophylactic one, since the cancer tissue which was transplanted received no treatment at all but only the tissue into which it was inoculated was so treated.

Later, Murphy, Maisin, and Sturm repeated somewhat similar experiments using spontaneous cancer instead of transplants, with the idea that such spontaneous tumours more nearly approximated the condition found in human cancer and would therefore provide more trustworthy data.

Experiment.—A mouse with a spontaneous mammary cancer was operated on with removal of the tumour. With the tumour out, an area on the left flank was exposed to an erythema dose of x-rays, after which a portion of the original cancer was reinoculated in the area so treated, and a similar graft was at the same time inoculated into the right flank which had previously been protected from x-rays.

Among forty-nine mice subjected to this treat-

ment, the graft failed to grow in the treated area in 71 per cent, while in the untreated area the grafts failed to grow in only 16 per cent—in other words, the simple raying of the field of operation in which the graft was inoculated conferred upon that mouse an immunity of 70 per cent against the cancer. Further, autografts of spontaneous cancer, established and growing in the skin disappeared in 76 per cent of the animals after an erythema dose of x-rays, whereas in animals in whom this treatment had not been administered similar autografts grew progressively in 96 per cent of the animals.

Even allowing for the difficulty of translating the observations made during animal experimentation into terms applicable to the human body, these experiments are exceedingly striking. If it is possible with a remarkable uniformity to protect mice against their own cancer by the use of prophylactic radiation, surely it must also be possible by applying some modification of the same method to protect the human subject.

However, before it is possible to form any accurate estimate of the value of such a method in its actual application it will be necessary to compare the results so obtained with the results of other methods of treatment. The surgical treatment of cancer of the breast forms the whole background upon which such a comparison must rest, and if it can be shown that the general results are improved by the use of x-rays in conjunction with surgery, then this improvement must be due in part to the x-ray treatment as well as in part to improved technique and earlier operation.

The statistics upon the subject of late results of surgical treatment vary within such wide limits that it is difficult to make use of them for this purpose. Some writers include only those cases operated upon early and without axillary involvement, and thus are able to report a high percentage of cases free from disease five or more years after operation. Others include a few recent cases or those in whom there is some doubt as to the malignancy.

A representative group has been exhaustively analysed by Burton J. Lee quoting from the records of the New York Hospital during a period when the radical operation was done

by very competent surgeons and when x-rays were not in use to any extent, and certainly not in a manner which can be compared to their present efficiency. I take the liberty of quoting Lee's figures. At the end of the five year period only 15 per cent of the cases were alive and well, and of the cases showing malignant involvement of the axillary glands at the time of operation only one was living. At the end of the three year period 35 per cent of the cases were living and well.

Other results quoted by Lee are as follows:

Haggard and Douglass.....	46%
Sistrunk and McCarthy.....	39%
Peck and White.....	39%
Tixier	38%
Bunts	33%
Greenough and Simmons	32%
Lindenberg	28%
Weisman	23%
Ochsner	22%
Lee and Cornell	15%

Sampson Handley (2nd Ed'n. 1922, page 217) reports that in thirty-one cases operated upon before 1910, 48 per cent survived the three-year period, and of these 80 per cent were in good health when last seen or heard from. He does not publish five-year results owing to the difficulty of tracing the cases. Moreover, all of his cases received prophylactic radiation as a post-operative measure.

Thus we are justified in the conclusion that surgical results may be called "good" only in those cases in whom the disease is a purely local disease confined within the breast. The moment the disease ceases to be local and the axillary glands are invaded the whole complexion of the problem is changed, and if the supraclavicular glands are involved the case is usually inoperable and hopeless.

It is because we are convinced that radiation methods can be of such great assistance in the two latter groups of cases that the question of operability is raised here. Ordinarily, the surgeon must be the final and only judge as to the operability or otherwise of any tumour. It is worse than folly to operate upon an advanced carcinoma of the breast merely because it is mechanically possible of removal, and then expect radiation to prevent the recurrence which is sure to come.

X-ray Therapy of Breast Carcinoma.—The x-ray treatment in this condition has gone through several stages of development and is

still far from reaching the fullest perfection of which it gives promise. In the early days the doses were fractional and chiefly of value as a very superficial application. As apparatus improved, its usefulness also improved. Then came the highly penetrating rays with the teaching of certain continental schools that the whole massive dose must be given at a single sitting in order to be effective and must be pushed to a rather extreme limit.

From the standpoint of physics and the measurement of the dosage this was undoubtedly along the right line, but it was soon discovered to be subject to at least two very serious faults clinically.

(1.) The first of these consisted in the production of fibrosis of the lung. This fibrosis is probably a secondary process to lymphatic stasis and fortunately occurred in only a small percentage of cases which did not receive multiple doses or too severe cross-firing of the lung. As soon as it was recognized as a possibility as a sequel to x-ray treatment the technique was modified in a manner which will be described under that heading, so that at the present time (in our own work) the lung does not receive this intensive radiation and is never cross-fired.

(2.) The second disadvantage is due to overdosing at a single exposure, or to too frequently repeated raying of the chest wall. It appears to bring about a lowering of the resistance of the normal tissue to the growth of the cancer cell, resulting in their more rapid growth within the confines of that particular area of skin. This phenomenon has occasionally been wrongly interpreted as stimulation of the growth of the cancer cells. The result is undoubtedly the same but we believe the mechanism by which it is brought about is not stimulation of the cancer, but rather the removal of certain barriers already existing.

This possibility is emphasized in order to guard against it as a source of danger and because it points us directly to the proper selection of dose and technique. We have only once seen this condition develop in any case which received a minimum erythema. In the experiments on mice reported above, the dose which protected and raised the resistance of the tissues against cancer cells was the minimum erythema. Evans writing in the *American Journal*

of *Röntgenology* has pointed this out and our own experience agrees entirely with his, viz; that when x-ray treatment is given for prophylactic purposes the dose administered should not exceed a minimum erythema. As soon as this is exceeded we get beyond the period of stimulation and soon reach a point where it is possible to depress and devitalize the normal tissues.

Having adopted a method based upon these ideas and followed it consistently since the early months of 1922 we have analysed the results of all cases treated during the year 1922. We admit that three year period is too short a period to justify sweeping conclusions and yet it is probably not too short a period to suggest tendencies and from which to learn a few important lessons.

There were 108 cases treated during this period, of which at this time we were unable to secure accurate information regarding twenty-one. The remaining eighty-seven are shown according to the following table:

TABLE I.

Prophylactic, post-operative.....	37
Pre-operative radiation	1
Radiation treatment not followed by operation	4
Inoperable, treated for palliation only	7
Post-operative recurrences	38
	<hr/> 87

Of the thirty-seven cases treated for prophylactic purposes the majority are known to have had malignant involvement of the axilla at the time of operation. Cases in whom the carcinoma is a purely local disease with no glands in the axilla are not usually referred for post-operative treatment. The result is that certainly 80 per cent of these cases may be considered to have had axillary involvement although our records are not exact on this point to within 10 per cent.

At the present time the situation regarding these thirty-seven cases stands as follows:

TABLE II.

Living and well, no evidence of disease..	22
Dead	13
Known to have recurrence (one is a recurrence in the other breast. May be new disease?).....	2
Total	<hr/> 37
Percentage free from disease 3 years....	59.4%

One other case was an inoperable large mass which under treatment became operable and was successfully removed.

Four cases were operable but for one reason or another operation was not considered advisable, and these were treated by radiation. In three the masses entirely disappeared, the fourth was improved temporarily and apparently greatly retarded in its rate of growth.

Seven cases which were quite inoperable and hopeless were treated for palliation only.

TABLE III.

Treated for palliation only.....	7
Became operable and was removed.....	1
Healed but developed secondaries in other parts of body.....	2
Not improved	2
Improved temporarily.....	2
	<hr/> 7 <hr/>

The following we believe a fair summing up of the situation as it stands at the present time:

Average of results as reported by ten different surgeons....	31.5%
Corrected for 3 year period would be	35%-40%
Average of similar group of cases when treated by radiation....	59.4%

If this is an accurate conclusion then the treatment has given an added protection to that group of patients equal to approximately 25 per cent. Lee's figures which are very carefully worked out, give a percentage at his three year period of 35 per cent.

Treatment of Post-Operative Recurrences.

Thirty-eight cases in the present series presented themselves for treatment with established recurrences as follows:

Local recurrences in chest wall.....	4
Axillary and supra clavicular.....	26
Metastases to bone (sternum, ribs, spine)...	3
General	5

These may be briefly summarized by saying that of the thirty-eight there are five living and apparently free of disease. The lesions for which treatment was undertaken have completely disappeared, and there is no evidence at the present time of recurrence.

Three others survived for three years at the end of which time the disease extended and proved fatal. Five survived in a similar way for two years while nineteen died within one year or less from the time of treatment.

There is thus no ground for much optimism

as to the possible results of treatment of such cases as these, and yet a review of the case histories yields some exceedingly interesting information and this we believe is decidedly encouraging.

Local Recurrences on the Chest Wall.—In local skin recurrences the method of treatment adopted will depend upon whether the recurrences are single nodules or many. In all cases in which the number of nodules is not too great, we treat each nodule with a surface application of radium and in addition we use modified x-ray treatment over the entire chest wall, back, front and side, while the axilla and supra-clavicular areas receive high voltage x-ray. By this method the majority of such recurrences will promptly disappear. But if the lymphatic spaces are well seeded with recurrences they will sooner or later reappear, or others will appear, and only in a few cases, and by careful persistent effort can they be completely eradicated. These cases require the greatest co-operation on the part of both the patient and the patient's physician or surgeon. The early results are usually excellent, and in a few cases quite spectacular, but this must be followed up by very close observation and further treatment at the first sign of return.

Axillary and Supra-Clavicular Recurrences.

Of these there were 26 in this series of cases. In the majority of these cases both groups of glands were involved as follows:

Axilla and supra-clavicular.....	12
Axilla alone.....	19
Supra-clavicular alone.....	4

However, there is always so much difficulty in being certain of such facts clinically that in all cases in which palpable nodules were present in either axilla or supra-clavicular region we have treated both these areas.

In practically all cases the treatment has consisted in a combination of heavy radiation with radium packs together with intensive x-ray by the high-voltage method.

Of these twenty-six cases a few showed no sign of any improvement whatever, went progressively down hill and died. Five of the cases were complicated also by metastases in the pleura or the lung. In these very little real improvement could be said to have occurred. But in all the others the improvement was marked and varied all the way from a

moderate degree to complete disappearance of the nodules. As has already been reported in five of these this appears to be permanent. And while this represents only 13 per cent of results which might be called successes yet that 13 per cent has occurred in otherwise quite hopeless cases.

In these cases as in the local skin recurrences very careful watching is essential. These patients should be seen every month as a routine, and thoroughly searched for any sign of a return of the nodules. If no recurrence takes place we repeat the treatment in three months as a precaution. In this case the radium is frequently omitted, though this is a question which must be decided in each individual case.

Metastases to Bone.—One of the commonest sites for metastases to bone is the lumbar spine, and too much emphasis can scarcely be given this fact. If a patient has had a breast removed for carcinoma and later develops pain in the the back which persists, the spine should be studied for metastases even though it may be many months or even years since the operation. We have one record in which this developed seventeen years after the operation. The plates of the spine for this purpose must be good and the most useful view is the lateral. In addition to this, however, properly taken stereoscopic antero-posterior plates are essential.

The appearance of the lesion is fairly characteristic and consists in a destruction of the body of the vertebra to such an extent that it collapses but the process is a purely destructive one. The intervertebral discs are not involved.

In these cases, when the disease is well advanced, the pain is excruciating, and it is because of this that treatment is so important. There have only been one or two cases in a fairly large series which we have now treated, in which this pain has not been almost entirely relieved. In a few cases the relief has been lasting, while in others the treatment has been repeated at a later date. But in the majority, the relief has been very complete and has persisted until extension of some of the other lesions has carried the patient off. A small percentage of the cases have been exceedingly satisfactory, and in them there appears to be a chance of a cure in so far as the spinal lesion is concerned.

In other bones the results are, we believe, sufficiently encouraging to justify treating them so long as one does not lose sight of the fact that all such cases are merely stages in a general involvement, and there is little hope of radical cure. Lesions have disappeared from bones and the area has been recalcified in a sufficient number of cases to indicate that the discovery of bone involvement is not necessarily an immediately hopeless matter in which nothing of value can be done for the patient. If the lesion is single as in the sternum or the clavicle we have in several cases secured complete and apparently permanent healing with recalcification of the bone. If the lesions are multiple in the long bones the problem is more difficult and naturally less promising, but even here the most surprising and almost unbelievable regression of the disease and improvement in the condition of the patient may occur. An example of this is quoted below in history No. 2. It opens up too large a discussion both as to the reason for the improvement with so little radiation and as to the exact nature of the change which takes place in these cases to be followed in detail here.

Metastases in the lung and pleura.—While several writers have reported good results in such cases we have not shared that fortunate experience, and have to report that without exception cases having lung involvement have benefited little or not at all, and have all ultimately proved fatal. If the involvement is discovered in an early stage it may be that treatment will delay the rate of its progress. But whether this actually happens is a very difficult question to decide. In the later cases we have not succeeded in materially influencing the progress of the disease.

General Considerations.—The management of the radiation treatment of a case of cancer of the breast is at best a somewhat complicated procedure calling for qualities of technical training and a knowledge of pathology not possessed by all radiologists. We believe everyone seriously attempting this work should be equipped with both radium and x-rays and in the latter should be equipped with apparatus capable of operating at any desired voltage, from one hundred thousand up to two hundred or two hundred and fifty thousand volts. Under no circumstances should a non-medical person

be entrusted with the administration of this treatment except as the technical assistant of a qualified medical radiologist.

The radiologist here is called upon to modify this method to suit each individual patient just as the surgeon modifies the technique of each operation, and in doing this he should be given the fullest freedom and co-operation. There are still a few surgeons who by attempting to dictate their own wishes in these cases only succeed in tying the hands of the man who is being held responsible for the outcome of the treatment, in a manner which no surgeon would tolerate in his own work.

The Place of X-rays.—X-rays may be made to adequately cover a much larger area than the quantities of radium available to the average worker, and should, we believe be used in the majority of cases for purposes both of efficiency and economy.

(1) *In all prophylactic treatment.*—Here we limit the voltage used upon the chest wall or falling upon the lung to 140 K. V. and use 210 K. V. over the axilla and supra-clavicular areas.

(2) *Post-operative treatment.*—In practically all cases in which radium is used we also apply x-rays and find that in general one can administer three-quarters of a full dose of both radium and x-rays simultaneously without undesirably severe reactions, and with very decidedly better results.

The Place of Radium.—Radium is of value chiefly in dealing with accessible nodules in which an intense effect is desired.

(1) *Pre-operative Cases.*

(a) Small nodules single or multiple combined with x-rays in the form of surface application or packs.

(b) Buried platinum needles of low potency and high filtration are especially to be recommended. This method also may be combined with x-rays.

(2) *Post-operative Cases.*

(a) Small skin nodules treated by surface applications, plaques, packs or platinum needles on special wax moulds.

(b) Nodules in axilla. Needles may be inserted or packs may be used, depending upon the location and extent of the involvement.

(c) Supra-clavicular nodules packs are here indicated usually in conjunction with x-rays.

The greatest recent advance in the technique of radium application in these cases (as in buried radium generally) has been the introduction of the platinum needle method of Regaud. These applicators contain a relatively small quantity of radium element, usually one milligram and have a wall thickness of 0.4 m.m. platinum. This filtration is sufficient to filter out approximately 98 per cent of beta rays and all alpha rays, leaving for practical therapeutic purposes a pure gamma ray. The treatment is more satisfactory in its effects than buried emanation and entirely devoid of the sloughing and pain so commonly present in the latter method.

Up to the time of writing, these needles have been used chiefly in mouth cases but in the breast have been used in only two types. In each of these however the results have been so superior as to justify a much wider application.

The cases referred to are:

1. Small operable masses in cases which for one reason or another cannot be operated upon. In the same category are certain cases with masses in the breast (associated with axillary involvement) which can be completely included within the range of effectiveness of the needles.

2. Multiple small recurrences in the skin. The so-called "melon-seed nodules." This will be discussed in some detail below.

GROUP I.

It is our invariable practise to emphasize the importance of early operation in breast cancer and we have never accepted for treatment by radium or x-rays any such case unless operation was considered impossible by a reputable surgeon or had been definitely refused by the patient. Under such circumstances we feel perfectly justified in proceeding with radiation treatment and have so treated some twenty-five cases up to date of writing. The results are encouraging and will be reported in a group at a later date. The experience gained by the treatment of these cases has resulted in developing a procedure which with individual variations is as follows:

The first treatment is usually limited to x-rays and consists of exposing the primary tumour, the axilla and supra-clavicular areas, even though no glands may be palpable in the

latter. In this irradiation the so-called high voltage is used throughout. Over the breast an area is exposed which is large enough to include the breast only (if the breast be large and pendulous it is cross-fired) in such a manner as to expose as little of the lung as possible. In the large pendulous breast no lung is exposed. Following such a treatment there will be, in a majority of the cases, a marked regression of the growth. The erythema is moderate in intensity and has usually subsided so that a second treatment may be safely given in six to eight weeks time.

In a certain number of cases the tumours will disappear under x-ray treatments such as the above alone but the certainty of the procedure is not established and in those which disappear, some recur. In others, on the other hand a stage is reached where further regression does not take place, a mass still remains and if those cases are limited to x-ray measures they are almost certain to shortly take on renewed active growth from which time they fail to respond to further applications of x-rays however intensively these may be administered.

At the time when the benefit from the x-ray treatment is judged to have reached its maximum, radium in platinum needles is buried in and around the local mass in the breast.

The application is simple, consisting of the insertion under local anaesthesia of the required number of needles placing the needles at a distance of two c.m. from each other i.e., each needle will adequately irradiate a cylinder of tissue 1 c.m., in radius and approximately three c.m., in length. The only problem which presents itself is to place these needles accurately in such a manner that no tissue containing malignant cells escapes and none is over-treated. Using needles of such small radium content and having such high filtration values, the duration of the treatment is correspondingly prolonged. The average time in the breast has been four days i.e., 96 milligram hours per applicator. Under these conditions no sloughing has been observed and the clinical results have been excellent.

GROUP II.

Local Recurrences in the Skin.—In the past these so-called "melon-seed bodies" have given us a great deal of difficulty. Under x-ray treat-

ment they frequently, in fact usually, disappeared only to return later. Under treatment, again they disappeared but again recurred until finally they failed to respond and developed into a condition not unlike "cancer en cuirasse" of the entire side affected. We believe the use of platinum needles has resulted in a distinct advance. How completely it may prove to be possible to "sterilize" the skin without damage to the latter or whether this may be possible at all, is not certain at the present time. It can only be said that the results are greatly superior to any method we have previously used and merits further trial on a larger scale.

In making the application it is necessary to be in possession of a sufficient number of needles to cover a fair amount of skin surface at one time.

A mould of the chest wall affected is made, using dental modelling compound, and this is allowed to harden on the chest wall. It is then removed and the needles are embedded on the inner surface of the wax (i.e. that portion which will be in contact with the skin). The needles are distributed as evenly as possible over the area in which recurrent nodules are present bearing in mind the radius of effective action of each needle. They should be embedded in the wax merely deep enough to be retained in place and when all are in position are covered with a coating of paraffin 1 m.m. thick in the manner in common use in preparing such applicators in the mouth and elsewhere.

The mould, finally prepared, is then warmed slightly in warm water, quickly dried and applied firmly to the chest wall. The final warming permits it to be more accurately pressed into position where it is retained by strong adhesive strips for the necessary three to four days. The latter time will cause a rather intense erythema with vesication in an occasional case but has not been attended by other undesirable features. This time is recommended if the tissue is 1 c.m. thick or more but if the tissue is thin, seventy-two hours will be found sufficient without producing too severe a reaction.

Almost without exception the results have been entirely satisfactory, and are much superior to previous methods used. How per-

manent they may be still remains to be determined by the lapse of sufficient time.

ILLUSTRATIVE CASE HISTORIES

Case 1.—Inoperable carcinoma. Mrs. A. Admitted to the Surgical Service Toronto General Hospital and by them considered hopeless and inoperable. Referred to Radiology for palliative treatment. This proved to be a large mass, almost immovable upon the chest wall and having both axillary and supra-clavicular glands involved. The mass was treated by radium packs with high voltage x-rays while the axilla and supra-clavicular masses received x-rays only.

Three series of treatments in all were administered at the end of which time the axilla and supra-clavicular regions appeared to be free of disease. The breast was soft, flabby, movable and apparently normal except in the lower and outer quadrant where there was some thickening induration and indrawing of the skin. At this stage the patient was referred back to the surgical service and a radical operation was successfully performed. The patient is still alive and without evidence of recurrence.

Case 2.—Mrs. B. Radical operation two years before. Referred for "Sciatica" at which time plates of the spine and pelvis revealed extensive secondaries in the lumbar spine, ribs and pelvis. At this time patient was suffering the most intense pain, accentuated by the slightest movement. Treatment was administered during the month of October and was followed not only by relief of pain but by recalcification of all the known areas of involvement. During the winter following the patient lived a very active social life which included a great many dances and winter sports. Later the disease returned, this time involving the liver and mediastinum, failed to respond to any amount of radiation and proved fatal. The case is quoted to illustrate the relief of pain which is possible and which in itself is sufficient justification for the procedure.

Conclusion

This study has, we believe, demonstrated beyond any question the value of radiation not only as a post-operative prophylactic measure

but in the treatment of recurrences and, in selected cases, of the primary growth itself. The method permits of much greater improvement and perfection but how rapid this improvement may prove to be will depend in no small degree upon how fully the surgeon will recognize the facts which are being accumulated and presented by radiologists at large, and will co-operate in making this procedure available to his patients. Any measure which by any modification can be shown to improve the results of the treatment of breast carcinoma by 25 per cent should be a welcome adjunct to the surgeon and the medical profession at large.

Since the above was written and presented at the Canadian Medical Association meeting in Regina a study of the same problem has been published by Dr. Pfahler of Philadelphia, covering 801 cases and a period of twenty-five years. This paper is so full of interesting data and facts that it should be read in detail by every student of this problem. He summarizes his conclusions as follows: Of all cases, early and late, operable and advanced, inoperable and recurrent, 50 per cent were alive after three years, and 27 per cent after five years or more. In the post-operative group, without gland involvement, 81 per cent were alive after three years, and 77 per cent after five years or more. In the post-operative group, with gland involvement, 56 per cent were alive after three years, and 38 per cent after five years or more.

Problems of Child Life.—The factors contributing to dead births, premature births, and neo-natal births have been studied by a group of workers at the Royal Maternity Hospital, Glasgow, who found that in a series of over 500 infants examined neo-natal death was due to disease or malformation of the child in about 16 per cent, to the complications of labour in about 33 per cent, and to maternal disease in about 50 per cent. The same group of investigators at Glasgow have continued their studies of the toxæmias of pregnancy, on which subject a full report is nearing completion. The results indicate that in all forms of toxæmia in the second half of pregnancy there is a disturb-

ance of both kidney and liver functions, but the variations within each clinical group are so great that biochemical analyses of the kind made have given little help for the prognosis for individuals. A similar investigation is being carried out in Edinburgh in which the values of different tests of liver and kidney function in diagnosis, prognosis, and treatment are being assessed. Numerous investigations are in progress with regard to metabolism of infants, rheumatism in children, and rickets and tetany, but these have not yet been brought to the stage of yielding conclusions.—Report Medical Research Council, *Brit. Med. Jour.*, Jan. 23, 1926.

THE INFLUENCE OF DIHYDROXYACETONE UPON THE BLOOD SUGAR AND GLYCOSURIA*

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EVIDENCE that ingestion of the triose, dihydroxyacetone, would result in a lowering of the blood sugar in normal men, and that in diabetics the increment increase resulting was less than after a similar dose of glucose, was first presented by Isaac and Adler¹. This has been confirmed by Rabinowitch^{2 & 3} who has reported that if the dihydroxyacetone administration is equal to or less than the fasting carbohydrate utilization rate there is rarely any rise in the blood sugar level, but that a gradual fall takes place.

These observations have been confirmed in this clinic. In the present communication are reported further studies of the effect of dihydroxyacetone upon the blood sugar level, and in short time experiments upon the glucose excretion rate.†

Technique.—The blood sugar time curves were started at eight or nine in the morning on a fasting stomach. Fluid intake was constant throughout at the rate of 200 c.c. per hour. An attempt was made to perform identical curves on the same patients with both glucose and dihydroxyacetone. In a few cases this was impossible. The blood sugars were determined by the Folin and Wu⁴ method. Dihydroxyacetone was determined qualitatively in the blood and the urine by applying the fact that it will reduce alkaline copper solutions in the cold. In the glucose excretion experiments all the urinary sugar is calculated as glucose, Benedict's quantitative solution being used for its determination.

BLOOD SUGAR TIME CURVES—NORMALS

By Mouth.—Dihydroxyacetone ingested by normal individuals in amounts varying from 25

to 50 grammes results in a very slight increment increase in the blood sugar during the first one half to one hour, after which the blood sugar drops to a low basal level. Glucose in the same dose produces a greater increment increase which is of a longer duration. When dihydroxyacetone is given at the rate of two grammes every fifteen minutes for two hours there is no early rise in the blood sugar but a progressive decline takes place.

By Rectum.—When administered by rectum, 25 grammes at one injection, the effect upon the blood sugar is practically the same as after a like quantity of glucose. These results are shown in Table I, and in the main confirm the previous observations of Isaac and Adler¹ and Rabinowitch^{2 & 3}.

DIABETES MELLITUS

By Mouth.—In Table II are recorded twenty observations upon eight diabetic patients. The results show that in all cases except determinations 18 and 19, there was a much greater increment increase in the blood sugar after glucose than after dihydroxyacetone ingestion when given in 25 to 50 gramme doses. Also, the return to the fasting level was much accelerated in the case of the latter. In the case of No. 24, a moderately severe diabetic, there was very little rise after 25 grammes of dihydroxyacetone. Nos. 27 and 28 were children, both being practically complete diabetics. Nos. 18 and 19, an adult male with moderately severe diabetes showed a slightly less maximum increment increase after the dihydroxyacetone and the return to the fasting level was more rapid. When the dihydroxyacetone was given at a rate of two grammes every fifteen minutes (8 grammes per hour), practically a normal carbohydrate utilization rate, in most instances there was very little increase in the blood sugar. In Nos. 17 and 23 the blood sugar dropped below the basal

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† The dihydroxyacetone employed in this work was made by Farbwerke v. Meister Lucius and Brüning, Hoechst a. Main, and was supplied gratis by the Mallinckrodt Chemical Works, Ltd.

TABLE I
NORMAL: GLUCOSE AND DIHYDROXYACETONE BY MOUTH AND BY RECTUM

Det. No.	Case No.	Date	Blood Sugar—per cent							Remarks
			Basal	30 min.	60 min.	120 min.	180 min.	240 min.	300 min.	
1	42115	1925 April 21	0.091	0.123	0.130	0.114	0.107	0.097	Glucose: 50 gms.
2		April 23	0.092	0.107	0.082	0.082	0.089	0.089		Dihydroxyacetone: 50 gms.
3	41237	May 12	0.089	0.116	0.118	0.096	0.084	Glucose: 25 gms.
4		May 13	0.098	0.115	0.109	0.088	0.087	Dihydroxyacetone: 25 gms.
5		May 15	0.100	0.090	0.088	0.076	0.079	0.082	0.087	Dihydroxyacetone: 2 gms. every 15 min. for 2 hrs.
6	42513	June 18	0.093	0.086	0.083	0.073	Dihydroxyacetone: 25 gms.
7	41237	May 20*	0.109	0.099	0.094	0.072	0.087	Glucose: 25 gms.
8		May 18*	0.093	0.087	0.086	0.082	0.087	Dihydroxyacetone: 25 gms.

*Administration by rectum.

level while the dihydroxyacetone was being administered.

In one case, Nos. 20 and 21, there was practically no difference between the two curves. This was a young male, the diabetic condition being moderately severe. In chart I is shown graphically the several curves obtained in Case No. 42015, a moderately severe diabetic.

Intravenously.—Dihydroxyacetone administered intravenously in 25 gramme doses to two adult diabetics has shown little effect upon their blood sugar levels. (Table III Nos. 29 and 30). In both the triose could not be detected qualitatively in the thirty minute blood samples. These cases had a good carbohydrate tolerance. In another case No. 31, a boy aged 16 years, a severe diabetic recovering from a period of ketosis, showed a moderate rise (0.423 to 0.459) in his blood sugar after a five-gramme intravenous injection. However, the glucose excretion rate per hour was markedly decreased, falling from 17.2 grammes to an average of 10.5 grammes per hour for the next three hours. In the same case, two days later, injection of 5 grammes of dihydroxyacetone at the end of the basal hour and again in sixty minutes resulted in a more prolonged blood sugar rise. The average glucose excretion rate per hour for the next three hours averaged 8.1 grammes, only 0.6 grammes greater than that of the basal hour. The triose

was not detected in the blood. These results would indicate that in diabetics with a good carbohydrate tolerance dihydroxyacetone introduced intravenously is rapidly removed from the blood stream, being converted into some product which is probably not glucose. In severe diabetes this removal from the blood stream is impaired, and the percentage glucose content of the blood increases.

By Rectum.—By rectum in a 25-gramme dose, dihydroxyacetone in one diabetic showed practically the same effect upon the blood sugar as after the same dose of glucose. (Table III). Differing from the normal (Table I, No. 7 and 8) there was a slight rise in the blood sugar at the end of thirty minutes.

GLUCOSE EXCRETION AFTER DIHYDROXYACETONE

Realizing the difficulties involved in judging the effect of dihydroxyacetone ingestion upon the glucose excretion rate in short time periods the following results are presented. Such experiments to be conclusive should be controlled by observations for consecutive days with the patient upon a constant diet and having a uniform rate of glycosuria. The criticism that decreased excretion might be due to retention can be largely ruled out by assuming that fifty per cent of the total body weight is in diffusion equilibrium with the blood. That dihydroxyacetone

TABLE II
DIABETES MELLITUS: GLUCOSE AND DIHYDROXYACETONE BY MOUTH

Det. No.	Case No.	Date	Blood Sugar—per cent							Remarks
			Basal	30 min.	60 min.	120 min.	180 min.	240 min.	300 min.	
9	42015	1925 May 27	0.182	0.184	0.176	0.170	Control
10		April 24	0.130	0.210	0.280	0.285	0.242	0.198	Glucose: 50 gms.
11		April 27	0.117	0.226	0.218	0.188	0.164	0.146	Dihydroxy-acetone: 50 gms.
12		April 30	0.117	0.145	0.158	0.152	0.150	0.142	Dihydroxy-acetone: 2 gms. every 15 min. for 2 hrs.
13	42458	May 4	0.144	0.152	0.154	0.150	0.146	0.142	Dihydroxy-acetone: 2 gms. every 15 min. for 2 hrs.
14		June 23	0.260	0.300	0.303	0.309	0.255	0.243	Dihydroxy-acetone: 2 gms. every 15 min. for 2 hrs.]
15		June 9	0.246	0.264	0.339	0.303	0.261	0.254	Glucose: 25 gms.
16	42594	June 11	0.141	0.188	0.168	0.142	0.123	0.133	Dihydroxy-acetone: 25 gms.
17		June 22	0.121	0.127	0.130	0.128	0.109	0.092	Dihydroxy-acetone: 2 gms. every 15 min. for 3 hrs.
18		July 2	0.190	0.279	0.267	0.246	0.220	Glucose: 25 gms.
19	42435	June 30	0.228	0.279	0.306	0.252	0.231	Dihydroxy-acetone: 25 gms.
20		June 3	0.150	0.168	0.184	0.194	0.250	0.246	Glucose: 2 gms. every 15 min. for 3 hrs.
21		June 2	0.168	0.176	0.188	0.212	0.258	0.236	Dihydroxy-acetone: 2 gms. every 15 min. for 3 hrs.
22	42047	June 4	0.127	0.142	0.148	0.150	0.152	0.116	Glucose: 2 gms. every 15 min. for 3 hrs.
23		June 5	0.140	0.147	0.152	0.134	0.128	0.117	Dihydroxy-acetone: 2 gms. every 15 min. for 3 hrs.
24		June 9	0.147	0.150	0.154	0.150	0.130	0.123	Dihydroxy-acetone: 25 gms.
25	42372	May 26	0.168	0.188	0.244	0.276	0.384	0.321	0.296	Glucose: 2 gms. every 15 min. for 3 hrs.
26		May 23	0.162	0.166	0.186	0.226	0.218	0.198	0.184	Dihydroxy-acetone: 2 gms. every 15 min. for 3 hrs.
27	42051	May 2	0.306	0.218	0.238	Dihydroxy-acetone: 2 gms. every 15 min. for 2 hrs.
28	42109	May 1	0.244	0.266	0.282	0.300	0.288	0.224	Dihydroxy-acetone: 2 gms. every 15 min. for 2 hrs.

may exert a "toxic" action upon the kidneys will have to be judged from the urinary alterations.

A matter of greater difficulty is to correctly appraise the conversion value of dihydroxyacetone in terms of glucose. What happens to dihydroxyacetone in the body is not known. At best we can speculate, but theorising to be profitable must be based upon facts. Reported studies indicate that the following main facts are known:

1. In phlorhizinized dogs dihydroxyacetone introduced subcutaneously is excreted quantitatively as glucose.⁵

2. In rats and mice after dihydroxyacetone feeding a much greater percentage of glycogen is found in the liver than after similar glucose feeding.¹

3. In both normal and diabetic individuals the blood lactic acid rises more after dihydroxyacetone than after the same dose of glucose. This difference is more marked when the dihydroxyacetone and the glucose are administered associated with a like dose of insulin.¹

4. In both normal and diabetic individuals dihydroxyacetone by mouth causes a much less increment increase in the blood sugar than after the same dose of glucose.^{1, 2 & 3}

5. Dihydroxyacetone by mouth causes a greater and more rapidly attained increment increase in the respiratory quotient in both normal and

diabetic individuals than does the same dose of glucose. (Personal studies).

6. Dihydroxyacetone by mouth causes a greater and more rapidly attained maximum heat production than does the same dose of glucose. This is true in both normal and diabetic individuals. (Personal studies).

If dihydroxyacetone is primarily converted quantitatively into glucose by polymerization such a marked difference from glucose in its effect upon the respiratory quotient and total metabolism would not be expected. Further it would be difficult to explain the immediate increase in blood lactic acid.

Conversion of dihydroxyacetone into lactic acid would explain the known facts much more satisfactorily. That the normal pathway of the intermediary metabolism of muscle glycogen is to lactic acid via a hexosephosphate, and that this reaction is a reversible one seems most probable from the researches of A. V. Hill and his associates.⁶ Further their work indicates that about four-fifths of the lactic acid formed is reconverted into glycogen, the major part of the heat produced from carbohydrate combustion coming from the oxidation of the lactic acid not participating in the reversible reaction.

The known changes taking place in the normal and the diabetic individual after the ingestion of dihydroxyacetone would be compatible with this theory. The sudden increased production

TABLE III
DIABETES MELLITUS: DIHYDROXYACETONE INTRAVENOUSLY AND BY RECTUM

Det. No.	Case No.	Date	Blood Sugar—per cent					Glycosuria		Remarks
			Basal	30 min.	60 min.	120 min.	180 min.	Basal hour	Total ounce test hours	
29	42015	1925 June 13	0.246	0.252	0.224	0.222	gm. 0	gm. 0	Dihydroxyacetone: 25 gms.
30	42047	June 11	0.136	0.154	0.130	0.112	0.102	0	0	Dihydroxyacetone: 25 gms.
31	42109	June 6	0.423	0.459	0.450	0.405	0.399	17.24	31.51	Dihydroxyacetone: 5 gms.
32		June 8	0.315	0.381	0.399	0.441	0.381	7.55	24.34	Dihydroxyacetone: 5 gms. at zero hr.: 5 gms. at 1 hr.
33	42015	May 26*	0.190	0.194	0.194	0.182	0.174	Glucose: 25 gms.
34		May 22*	0.210	0.218	0.194	0.178	0.168	Dihydroxyacetone: 25 gms.

*Administration by rectum.

TABLE IV
DIABETES MELLITUS

Kyle Case No. 42502 Glucose excretion after Dihydroxyacetone

Date Time	Intake		Urine			Blood		
	Water	Dihydroxy- acetone	Vol.	Glucose	Dihydroxy- acetone	Time	Sugar	Dihydroxy- acetone
1925	c.c.	gm.	c.c.	gm.			per cent	
June 13								
8.00 to 10.00	400		190	5.57	0	10	0.300	0
10.00 to 12.30	400	40	215	5.25	0	12	0.372	0
12.30 to 2.30	400	40	210	5.92	0	1	0.387	0
2.30 to 4.00	400	30	242	7.58	0	2	0.372	0
4.00 to 6.00	400	40	435	14.97	0	3	0.375	0
						4	0.390	0
Total:						5	0.312	0
(10 to 6) =		150		33.72		6	0.333	0

TABLE V
DIABETES MELLITUS

Clayton Case No. 42109 Glucose Excretion after Dihydroxyacetone

Date Time	Intake		Urine			Blood		
	Water	Dihydroxy- acetone	Vol.	Glucose	Dihydroxy- acetone	Sugar	CO ₂ Capacity	Dihydroxy- acetone
1925	c.c.	gm.	c.c.	gm.		per cent	vols. per cent	
April 28								
8.00 a.m.	200							
9.00 }	240	9 to 11	55	0.55	0	0.236	27	0
		3.3 gm. every						
9.30 }		10 minutes	85	1.60	+	0.262	..	0
10.00 }						0.327	..	0
10.30 }	240					0.393	..	0
11.00 }		11 to 1	338	4.54	0	0.414	48	0
11.30 }	200	2 gm. every				0.462	..	0
		15 minutes						
12 N. }			183	6.14	0	0.426	..	0
1.00 p.m. }	200		288	5.01	0	0.408	..	0
2.00 }	...		176	3.31	0	0.369	..	0
Total (9 to 2)		55.6		20.10				

of lactic acid would increase the blood lactic acid, cause a moderate increase of the blood sugar, and through the character of the reversible reaction cause an increased storage of glycogen in the liver; and by its partial oxidation markedly raise the respiratory quotient and the total metabolism. To explain the fact, in accordance with this theory, that phlorhizinized dogs excrete dihydroxyacetone quantitatively as glucose, it would be necessary to calculate that all the dihydroxyacetone is converted into glycogen or glucose through the intermediate stage of lactic acid.

Since in the normal and diabetic individual it would appear that dihydroxyacetone is most probably not converted quantitatively into glucose no conversion equivalent has been assumed in reporting the subsequent cases. In all instances a simple balance has been drawn between the dihydroxyacetone ingested and the glucose retention and excretion.

With these limitations in mind four short period observations upon three cases of diabetes mellitus are reported. At the time of the experiments three of the cases had varying degrees of ketosis. In no case was there evidence

TABLE VI
DIABETES MELLITUS

Clayton

Case No. 42103

Glucose Excretion after Dihydroxyacetone

Date Time	Intake		Urine			Blood	
	Water	Dihydroxy- acetone	Vol.	Glucose	Dihydroxy- acetone	Sugar	Dihydroxy- acetone
1925 June 19	c.c.	gm.	c.c.	gm.		per cent	
8.00 to 9.00	200		113	4.73	0	0.312*	0
9.00 to 10.00	200	10†	119	4.76	0	0.327	0
10.00 to 11.00	200	10	162	6.85	0	0.378	0
11.00 to 12.25	200	10	212	8.96	0	0.378	0
12.25 to 1.00	200	10	175	7.55	0	0.441	0
1.00 to 2.00	200	5	129	5.35	0	0.459	0
Total (9 to 2)		45		33.47			

*Blood sugars taken at end of each hour.

†Dihydroxyacetone 5 gms. every 30 minutes.

TABLE VII
DIABETES MELLITUSCharron. Case No. 43406 Glucose Excretion after Dihydroxyacetone and Na_2HPO_4

Date Time	Intake			Urine				Blood	
	Water	Dihydroxy- acetone	Na_2HPO_4	Vol.	Sp. Gr.	Glucose	Dihydroxy- acetone	Sugar	CO_2 Capacity
1925 November 3	c.c.	gm.	gm.	c.c.		per cent gm.		per cent	Vols per cent
4.30 p.m.	400	4	1	560*	1034	4.18 23.5	0	0.300	26.7
5.00		4	1						
5.30	400	4	1	420	1032	3.53 14.8	trace	0.297	28.8
6.00		4	1						
6.30	400	4	1	600	1024	2.56 15.4	trace	0.255	32.5
7.00		4	1						
7.30	400	4	1	720	1006	0.54 3.9	0	0.309	34.7
8.00		4	1						
8.30	400	4	1	180	1006	0.41 0.7	0	37.3
9.00		4	1						
9.30	400	4	1	250	1010	0.60 1.5	0	0.300	43.0
Total (4.30 to 9.30)		44	11			36.3			

*Approximately a two hour urine.

of renal irritation, as judged by urinary alterations. In two a trace of dihydroxyacetone was detected in the urine during the early period of its administration.

The first experiment (Table IV) was upon a female diabetic, aged sixty-one, admitted with marked ketosis, the plasma CO_2 capacity being 13.7 vols. per cent. A two-hour specimen of urine obtained at 10 a.m. contained 5.57 grammes of glucose and the blood sugar was 0.30 per cent. Dihydroxyacetone, 5 grammes every fifteen minutes were given by mouth for the next eight hours. During this period the glucose excretion rate increased slightly, there being a corres-

ponding rise in the blood sugar level. The latter by 6 p.m. had almost returned to the admission concentration. During eight hours (10 a.m. to 6 p.m.) with the ingestion of 150 grammes of dihydroxyacetone 33.72 grammes of glucose were excreted. Allowing that fifty per cent of the two hour basal glycosuria rate would have continued throughout the experimental period, the extra glucose excreted was 22.58 grammes. Since the final increment increase of the blood sugar was only 0.033 per cent, and the patient's weight was 70 kilos, assuming that 50 per cent of her weight was in diffusion equilibrium with the blood, the retention in the body would be

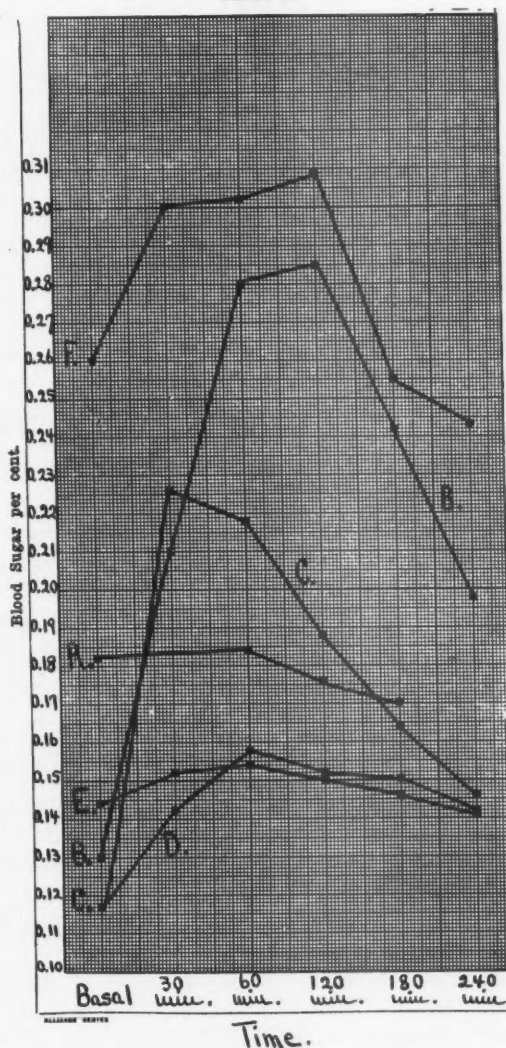
11.55 grammes. This would still leave an unexplained deficit of 115.87 grammes of dihydroxyacetone.

In Tables V and VI are reported data on a severe male diabetic. Shortly after recovering from a period of ketosis a moderate acidosis could be precipitated at will by discontinuing the insulin for twenty-four hours. In Table V are recorded the findings after discontinuing the insulin on April 27th. During the control hour the glycosuria was 0.55 grammes, the blood sugar 0.236 per cent, with a plasma CO_2 capacity of 27 volumes per cent. Dihydroxyacetone 3.3 grammes every ten minutes for two hours, then 2 grammes every fifteen minutes for another two hours were given. The five hours (9 a.m. to 2 p.m.) glycosuria was 20.1 grammes. The blood sugar level at 2 p.m. was considerably raised, 0.369 per cent. Assuming that 50 per cent of the body weight (37 kilos) would be in diffusion equilibrium with the blood the body retention would be 24.6 grammes. Allowing that 50 per cent of the basal glycosuria rate would have remained constant, the extra glucose excreted was 18.73 grammes. Therefore 12.27 grammes of the dihydroxyacetone ingested would still be unaccounted for. At a later period in the treatment of this same case observations were obtained after giving dihydroxyacetone, 5 grammes every thirty minutes for four and one-half hours, Table VI. The patient's weight now being 40 kilos, and as the blood sugar increased from 0.312 to 0.459 per cent, the total retention in the body was 29.4 grammes. Calculating that fifty per cent of the basal hour glycosuria rate would have remained constant, the extra excretion of glucose was 21.65 grammes. Therefore, 6.05 grammes of glucose were excreted which could not be accounted for.

In view of the recent work indicating that phosphates take an active part in the intermediary metabolism of carbohydrate, a case of diabetes with a moderate ketosis was given 4 grammes of dihydroxyacetone with one gramme of disodium hydrogen phosphate every thirty minutes for five hours, Table VII. The control glucose excretion rate was approximately 11.8 grammes per hour. A marked fall in the glycosuria occurred after the second hour, the total five hour (4.30 p.m. to 9.30 p.m.) glucose excretion being 36.3 grammes. The blood sugar fell slightly to

return to the control level of 0.300 per cent, eliminating the factor of tissue and blood retention. The ketosis was abolished. By similar calculations the extra glucose excreted was 6.8 grammes during the ingestion of 44 grams of dihydroxyacetone.

CHART I.



A chart comparing the several blood sugars curves in a case of diabetes mellitus (case No. 42015, Table II).

A.—Control.

B.—Glucose; 50 gms.

C.—Dihydroxyacetone; 50 gms.

D.—Dihydroxyacetone; 2 gms. every 15 min. for 2 hours.

E.—Dihydroxyacetone; 2 gms. every 15 min. for 2 hours.

F.—Dihydroxyacetone; 2 gms. every 15 min. for 2 hours.

Summary

In patients with a normal carbohydrate tolerance, the ingestion of dihydroxyacetone in 25 or 50-gramme doses results in a very slight transitory rise in the blood sugar. When it is given in small interrupted doses there is a progressive fall.

In diabetes mellitus the increment increase in blood sugar is not as great after dihydroxyacetone as after a like dose of glucose. When introduced intravenously in a dose of 25 grammes, diabetics, with a fair carbohydrate tolerance, show very little rise in the blood sugar.

Dihydroxyacetone ingested in small but frequent doses in three cases of diabetes mellitus in short period experiments could not be ac-

counted for by the glucose excretion and the tissue retention. The results are suggestive that in certain cases of diabetes mellitus the ingested dihydroxyacetone is not quantitatively converted into glucose.

I wish to gratefully acknowledge the technical assistance of Miss Helen MacLennan who performed the blood sugar estimations.

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THE DEFINITION AND CLASSIFICATION OF THE PSEUDO-LEUKÆMIAS*

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THE hæmatopoietic system, which includes as its organic entities the bone-marrow, spleen and lymph glands, presents certain unique features which add to the difficulties of its special pathology. In the first place, it is widely distributed, and hence cannot be examined in its entirety as the heart, lungs, etc. Secondly, it is composed of restless, constantly proliferating tissue. And, thirdly, it is subject to great age-period changes. These features have lead, in the past, to many wrong conclusions, which are reflected in the confusion of terms which pervades hæmatology to-day. Names of diseases based on past conceptions, later proved to be erroneous, are preserved, though they are no longer proper or adequate. And so there has developed, in the course of years, what practically amounts to nosological chaos.

One of the most striking examples of such a situation surrounds the term "pseudo-leukæmia", and it is for this reason and in hopes to aid in putting its use upon a rational basis,

that I have brought up the subject for discussion.

A consideration of the definition and classification of the pseudo-leukæmias naturally divides itself into three parts: first; the history of the development and use of the term; secondly, its definition and limitations in the light of our present knowledge; and thirdly, the application of this conception for the purpose of division and classification.

Historical consideration dates back nearly one hundred years. Up to that time occasional isolated cases had been described, which showed enlargement of lymph glands and spleen, with anæmia, cachexia, and a progressive, fatal course. In 1832, however, Hodgkin¹ reported seven such cases, and to him is due the credit of first carefully describing and grouping off as a disease entity this interesting clinical picture. We now realize that in all probability some of his cases were not, in truth, the condition which later, and even still, bears his name,—and very likely several different diseases were represented in his original group.

* Read before the Osler Reporting Society, Montreal, January, 1926.

Wilks² later described several similar cases and first introduced the term "Hodgkin's disease." Virchow,³ very early in his work, pointed out the multiplicity of conditions grouped under this name, and advised its dismissal. Wunderlich⁴ described such cases under the name "progressive, multiple lymph-gland hypertrophy", and Billroth⁵ introduced the term "malignant lymphoma". Other names followed, based upon the conceptions of the various authors as to the true nature of the condition. So there rapidly developed a conglomeration of nomenclatures to cover a number of different diseases, all presenting the same general clinical picture of glandular swelling and fatal course.

Toward the middle of the last century, with the advent of cellular pathology and the discovery and study of the blood cells, new complications arose. In four articles appearing at this time, Virchow^{6,7} separated certain diseases showing "white blood" from pyæmias and introduced the term "leukæmia". It was several years later, in 1865, that Cohnheim⁸ described a case in which, without leukæmic blood changes, all of the usual and characteristic tissue changes of lymphatic leukæmia were present. For this condition he introduced the term "pseudo-leukæmia". Later there were described what were termed "aleukæmic leukæmias of the myeloid type", that is, cases showing the typical histological tissue changes of myelogenous leukæmia, without the usual marked increase in white blood cells. So there developed rather gradually, during the following years, the conception of leukæmia as a tissue, not a blood, disease, and it was considered, quite rightly, merely a secondary matter whether the immature cells were discharged into the blood stream. This has lead recently, as I pointed out in a previous paper,¹² to a movement to reserve the term "leukæmia" for the blood changes, and substitute such terms as "leukosis", "lymphosis" and "myelosis" to designate the disease itself.

Following Cohnheim's introduction of the name "pseudo-leukæmia", various authors reported cases showing glandular and splenic enlargement without blood changes. Some adhered closely to the same histological tissue alteration; others did not. Considerable confusion arose, until finally the term lost for many its original meaning, and came to stand

for all conditions with enlargement of lymph glands and spleen, without leukæmic blood picture. That is, pseudo-leukæmia became synonymous with Hodgkin's disease, malignant lymphoma, etc., and thus still another name was added to this already large and indefinite list.

The height of confusion was reached toward the close of the last century; then the tangle began to unwind. First in 1893, Kundrat⁹ separated from this multiplicity of diseases with similar clinical picture, an anatomically well characterized condition to which he gave the name, "lymphosarcomatosis". Here a systemic lymphoid disease, lying in a sense between the leukæmias and the true neoplasms, was differentiated and isolated. Paltauf¹⁰ followed in 1896 with an attempt at classification and division on purely anatomical grounds. And soon after another condition, characterized by a granulomatous inflammatory process, was separated from the group, and given the name "lymphogranulomatosis". At a meeting of the Berlin Hæmatological Society in 1909, after numerous discussions, it was recommended to drop the term "pseudo-leukæmia" altogether. However, in subsequent meetings this decision has been publicly debated and revised, and the name remains with us, some employing it with the original meaning of Cohnheim, to designate an aleukæmic or subleukæmic leukosis; others to signify the clinical picture which this and several other conditions present.

In this historical sketch we have purposely omitted the introduction of the term "pseudo-leukæmia" in quite another sense. In 1890, Von Jaksch¹¹ first described anæmias in children characterized by a quite marked increase in the white blood cells. These may be comparatively immature and in such numbers that leukæmia is suggested, and he gave the name "anæmia pseudo-leukæmica infantum" to the condition. The term is thus employed, not in the sense of the clinical symptom complex, but rather because of the similarity of the blood picture. Moreover, the term has been used in yet a third way, namely in the description of histological tissue sections, to designate irregular hyperplasias and metaplasias which suggest the tissue changes of true leukæmias.

With this survey of the introduction and employment of the term "pseudo-leukæmia" in mind, we now turn to its definition in the light

of our present knowledge. First of all one thing stands out conspicuously, namely, that to avoid confusion and misinterpretation the term should be dropped as a name for any disease entity. Its very prefix "pseudo" suggests false conclusions, and, therefore, should never be employed to designate any recognized and specific pathological process. Secondly, its use, as long as it remains, should be strictly limited to the simple meaning of the word itself,—that is, *suggesting, bearing, certain resemblance to,*

PSEUDO-LEUKÆMIAS

I. CLINICAL

ALEUKÆMIC LEUKOSES.

LYMPHOSARCOMATOSIS.

NEOPLASMS.

INFLAMMATORY.

LYMPHOGRANULOMATOSIS

TUBERCULOUS

SYPHILITIC

NONSPECIFIC LYMPHADENOSSES.

LYMPHADENITIS,

II. HÆMATOLOGICAL

VON JAKSCH'S ANÆMIA, ETC.

III. HISTOLOGICAL

MYELOID METAPLASIAS.

STATUS LYMPHATICUS.

FÆTAL HYDROPS, ETC.

but not actually a leukæmia. We have found that this resemblance may come about in three ways, which may be termed clinical, hæmatological, and histological; clinical where the symptom complex resembles; hæmatological where the blood picture simulates, and histological where the tissue changes suggest a leukæmia. These, therefore, form the basis of our classification.

Clinically, pseudo-leukæmia stands for a quite distinct symptom complex. This consists of enlarged lymph glands with or without a palpable spleen and a normal, subnormal or only moderately raised white blood count. There usually is at least a moderate anæmia, and sometimes fever. When we enumerate the various conditions which may present this picture, we find we have included several distinct pathological entities which form the subdivisions of this group. These are the aleukæmic and subleukæmic leukoses, lymphosarcomatosis, genuine tumours involving the lymph glands in

multiple fashion, and certain inflammatory conditions.

Under the aleukæmic and subleukæmic leukoses, we group those leukæmias of the older terminology, in which there is not a marked increase in white blood cells. These are as a rule initial stages of the disease, and subsequently show typical high white cell counts. They may be of either lymphoid or myeloid type. Though there is no marked increase in leucocytes, differential counts as a rule show many immature forms and the diagnosis may, therefore, be made by the qualitative alteration. In the aleukæmic lymphosis, we encounter the pathological state to which the term "pseudo-leukæmia" was originally applied by Cohnheim.

Lying in a way between the leukoses and the typical tumours of the hæmatopoietic system, are two analogous conditions which on the myeloid side are termed "multiple myeloma", and on the lymphoid side "lymphosarcomatosis". While they have many of the features of true tumours, they possess systemic attributes and consequently are to be separated from typical neoplasms. The latter, lymphosarcomatosis, may present the pseudo-leukæmic symptom complex and consequently concerns us here.

The history of the identification of this condition and its separation from the other pseudo-leukæmic processes forms a most interesting chapter in hæmatological history, but can be only touched upon here. It owes its position as an entity first to the work of Kundrat, and then Paltauf while more recently Ribbert,¹³ Naegeli¹⁴ and Ghon and Roman¹⁵ have pointed out its distinguishing pathological characteristics. It consists essentially of the proliferation of relatively immature lymphoid cells which infiltrate the remaining lymphoid tissue of the gland, break through the capsule and invade adjacent organs. It lacks, however, the destructive tendency of true malignant tumours, and is rather a process of invasion and substitution. Its origin may be confined to a single group of glands, as the cervical, axillary, mediastinal, etc., or occasionally it is multiple and more systemic in nature. Then many gland districts are simultaneously involved and the pseudo-leukæmic symptom com-

plex is produced. Such a case is under observation in the Royal Victoria Hospital at the present time.

True multiple primary sarcomas of lymph glands have been described as in the cases of Troje¹⁶ and Baumgarten.¹⁷ They are extremely rare and generally of spindle cell type. Similarly multiple endotheliomas of lymph nodes have been observed. A pseudo-leukæmia in the clinical sense may be produced also, though very rarely, by the presence of multiple secondary metastases of cancers. Such a case of prostatic carcinoma¹⁸ has been reported by Lundsgaard¹⁸.

Finally, the pseudo-leukæmic complex may be produced by various inflammatory conditions. Of this group by far the most important is lymphogranulomatosis, often, though quite improperly, referred to as "Hodgkin's Disease." Here the lymph glands of the neck are as a rule first involved, but other organs soon follow. Moreover, the spleen is generally enlarged. The histological alteration in the involved nodes is that of a granulomatous inflammation, characterized by a marked pleomorphism and multiplicity of cell types. A great variety of pictures occurs from more pronounced hyperplasia in the early stages, to necrosis and fibrous connective tissue increase in the most advanced forms. Whether tuberculosis is the etiological factor in lymphogranulomatosis is still a disputed question amongst pathologists but such a conception seems to be gaining ground.

The simultaneous involvement of several groups of lymph glands by typical tuberculous lesions is not uncommon and has been termed "tuberculous pseudo-leukæmia". Often, however, the tissue changes are atypical and the true nature of the condition is only positively determined by the demonstration of the bacilli in sections or by animal inoculation. Moreover, confusing cases of multiple involvement of lymph glands in tertiary syphilis occasionally occur, and must be here included. They often soften and break down, but respond to specific treatment.

There must, in addition, be mentioned a large group of non-specific, septic, toxic and inflammatory conditions, occurring particularly in children, which are characterized by generalized glandular enlargement, with, occasionally,

an enlarged spleen. Apparently in early life, as mentioned above, these tissues respond with hyperplastic changes at the least provocation, and it is not uncommon to find such changes following the acute exanthemata. Here is to be included the acute lymph-adenosis, previously termed "infectious mononucleosis." Many of these conditions present marked increase and alteration in white blood cells, and are, therefore, likewise hæmatologically pseudo-leukæmic.

The differential diagnosis of the various conditions mentioned under this symptom complex rests in part on a very careful consideration of the history and course, but particularly on complete morphological blood examination. Many of the diseases may be thus definitely identified; in others, however, either there are no characteristic changes in the blood, or these have not been sufficiently studied to be of much value. In such doubtful cases excision of a superficial gland allows microscopic examination which as a rule settles the question, though the histological changes in lymph glands may present pictures, which offer difficulties in diagnosis. Morphological description may be comparatively simple, but positive diagnostic conclusions impossible.

Second: the hæmatological pseudo-leukæmias, are characterized by a blood picture which simulates that of a leukæmia. The presence of relatively immature cells, of both the lymphoid and myeloid series in considerable numbers in the blood stream is by no means a rare occurrence, particularly in children. At this age, because of the instability and activity of their hæmatopoietic tissues, immature forms enter the blood stream on the least provocation. Von Jaksch's anæmia is, therefore, but one of the results of numerous toxic and septic conditions in children, which produce pseudo-leukæmic blood pictures. In fetal life this is even more often the case than in childhood, for in intrauterine life leucocytosis, because of the immaturity of the cells, rapidly takes on the appearances of leukæmia. This has led to the erroneous diagnosis of "fœtal leukæmia" in many instances, particularly in cases of fœtal hydrops. But these often confusing cases are not confined to childhood. Severe anæmias in adults in the presence of good regenerative activity of the bone-marrow, and often with splenic enlarge-

ment, are not rarely characterized by many immature myeloid forms. Moreover, high counts are no positive criteria of the leukæmic state, for very high figures have been reported in other conditions, as for example: 112,000 in a patient with sarcoma, and Hirschfeld and Kothe's case of gangrenous appendix with a leukocytosis of 190,000. Similar very confusing blood pictures arise in certain chemical poisons as pyridin, nitrobenzol, etc., in dermatitis resulting from mercury as reported by Hoffmann, and in metastatic tumours involving the skeletal system. These *hæmatological pseudo-leukæmias* are often distinguishable only by very careful study and differential examination of the white blood cells, and even then may require repeated subsequent examinations before positive conclusions can be drawn.

Third: pseudo-leukæmias in the histological sense, are likewise much more common than is generally believed. Naegeli points out the difficulty which often confronts the pathologist even in autopsy sections of distinguishing extensive myeloid metaplasias in severe anæmias from genuine leukæmic processes, and suggests that many of the reported cases of leukæmia with low white counts are to be questioned. Several such cases have come to our attention, where only after the most careful cytological study and consideration of the extent and involvement of organs could conclusions be drawn. Here, just as in the previous group of leukæmoid conditions, confusing similarities arise frequently in childhood and in the fœtus. Status lymphaticus in atypical cases may present histological pictures bordering on a true lymphosis, and various authors have pointed out the intimate relation between the two diseases. Likewise myeloid metaplasia is very common and often extensive in the toxic and septic conditions of early life.

In the fœtus one disease stands out conspicuously in this connection, that is,—congenital dropsy or fœtal hydrops, which was mentioned above. This peculiar picture of generalized œdema occurring in premature infants, which are born dead, or die soon after birth, has been reported by many observers as a fœtal leu-

kæmia. We realize at present that, although the macroscopic and microscopic organ findings suggest such a diagnosis, we are most probably dealing with a disease of quite different nature, and that these tissue changes are merely the result of a peculiarly sensitive capability of reaction on part of the fœtal hæmatopoietic apparatus.

The classification outlined above impresses upon us the large number of diseases which may be included under the term "pseudo-leukæmia" according to its interpretations. Moreover, it emphasizes the necessity of dropping the term completely as a name for any specific disease. Even in the original sense of Cohnheim this effort would only lead to misunderstandings. The word is, however, so deeply rooted in medical literature, that it will no doubt persist for some time, but as long as it does it should be used only in the true meaning of the word itself, i.e., as a *descriptive term signifying a leukæmoid state*.

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HÆMOLYTIC JAUNDICE ASSOCIATED WITH SPLENOMEGALY

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TWENTY-FIVE years ago Sir William Osler drew the attention of the English-speaking public to the fact that there existed a type of chronic anæmia which differed materially from pernicious anæmia and which, while accompanied by marked enlargement of the spleen, was not attended by a leucocytosis. To this condition had been given the name "Splenic Anæmia." Since that time abundant evidence has been produced to show that the name "Splenic Anæmia" was one which covered a variety of diseases of very different origins, and to-day we are familiar with several distinct clinical entities under the names of Gaucher's splenomegaly, Banti's disease, congenital familial jaundice, acquired hæmolytic jaundice and von Jaksch's anæmia, and there is little doubt that further study and experience will result in the differentiation of other distinct diseases. While much is known in regard to these newer types of anæmia there is unfortunately a great deal yet to be learned, particularly in regard to the relation of the spleen to the disease and to the significance of its pathological enlargement. The importance of the spleen has been enormously increased from a clinical standpoint by the discovery that in certain cases its removal produces a spectacular relief from symptoms and in some an apparent cure. In the absence of complete knowledge of the physiology of the spleen and of the pathogenesis of the diseases grouped under the name of splenic anæmia the treatment of these diseases is necessarily somewhat empirical. While splenectomy is undoubtedly a great addition to surgical therapeutics, it must be admitted that the discovery of its value was purely a chance affair, and based on no rational process of reasoning. It is of the utmost importance, therefore, that before applying it to the treatment of any particular case, the greatest care must be taken in establishing a diagnosis in order that the operation may be limited to those types which are known to be benefited by it.

Chief among these is hæmolytic icterus or acholuric jaundice. This disease was first established as a clinical entity in 1898 by Hayem. He described a clinical picture which has since been established as characteristic, in which the patients acquire during adult life a chronic jaundice with the presence of bile-pigment in the blood but not in the urine, and without the usual signs of obstructive jaundice such as itching, slow pulse and clay-coloured stools. In quiescent stages there is a distinct anæmia with the red cells ranging from two to three millions, but, as pointed out by Widál, exacerbations are frequent and at such time the jaundice deepens and the anæmia becomes profound. It is in these so-called "crises of deglobulization" that many of the patients succumb.

A few years after the differentiation of this distinct disease from the group of splenic anæmias, Minkowski drew attention to a very similar condition occurring as a family disease and showing itself in early childhood. To this condition has been given the name congenital or familial hæmolytic jaundice. This disease resembles in a great many ways the acquired form of adult life, but there are also some distinguishing features, chief of which is that in the congenital form the patient, although decidedly jaundiced, is not sick, whereas in the acquired form the profound illness is much more important than the jaundice. We have under observation two cases, father and son, both deeply jaundiced from birth, who, except for a lack of animation and mental acuteness, have nothing to complain of more than the jaundice.

For some time following the publication of the papers of Hayem and Minkowski, hæmolytic icterus was described as occurring in two types, the acquired and the congenital or familial. As the number of cases reported in the literature increased, however, it was soon seen that no such clean-cut division into types

could be made. Thus it was found that sometimes the disease was congenital without any evidence of heredity, and without association with the disease in other members of the family. Again, the symptoms sometimes did not appear until late in childhood and even until adult life, although the disease may have been present in one of the parents and in other members of the family. The cases we have to report occurred in sisters aged thirty-seven and forty-nine, daughters of a man who had probably died of the same disease at fifty-four. It does not seem likely, therefore, that any division into types on such a basis, will lead to a further differentiation of distinct diseases. As an actual fact, a study of individual cases shows such an extraordinary similarity both in the clinical and pathological pictures that most observers are inclined to the view that all the types are variations of one and the same disease, and this view is strongly supported by the apparently curative effect in all of splenectomy.

While it seems probable that the various types of hæmolytic icterus with splenomegaly are in reality the result of a single form of disease, the symptoms and clinical signs have wide variations. As this paper has to do with one type only, however, we shall limit our further remarks solely to that type, namely the acquired form of adult life. This form of splenic anæmia usually commences with definite evidence of illness. Anæmia and its accompanying signs rapidly develop, and the red cells may fall to below 1,000,000. With the anæmia comes a chronic jaundice, which differs distinctly from obstructive jaundice in the absence of bile-pigment from the urine and of the usual symptoms of itching, brachycardia and clay-coloured stools. The spleen is found to be much enlarged and in some cases the liver is enlarged also. Examination of the blood shows a profound anæmia of the chlorosis type. A characteristic of great importance was noted by Chauffard, who showed that the resistance of the red blood-cells to hypotonic salt solution is much diminished. This fragility of the red cells can be demonstrated in the great majority of cases, but not in all. Increased microcytes and reticulated red cells and other signs of excessive blood-regeneration can frequently be seen. A test of some importance is the

auto-agglutination test of Widal. A drop of the patient's washed red blood-cells is mixed with ten drops of his own serum and, if the test is positive, agglutination of the red cells occurs in a few seconds. Widal claims that this test is positive in no other condition, although this is open to question. The evidence of excessive destruction of the blood can be confirmed by estimation of the urobilin excreted in the urine and stools.

After a period of profound anæmia the patient may show distinct improvement both in symptoms and in the blood-picture. It is characteristic of the disease, however, that severe relapses occur which have been called "crises of deglobulization," with the signs of excessive blood-destruction. In these crises there are intense malaise, fever ranging to 102 degrees, increase in the size of the spleen and a deepening of the jaundice. It is in such acute exacerbations of the disease that fatal terminations frequently result.

It is in this form of splenic anæmia that the removal of the spleen has given the most brilliant results. In 1915 Elliot and Kanaval collected sixteen cases of typical acquired hæmolytic icterus from the literature, and since then Mayo and others have added many more, in practically all of which apparent cures resulted. How these cures are brought about, our present knowledge of the pathogenesis of the disease does not explain, but the immediate and striking disappearance of the jaundice, the rise in the red blood-count and the return of the patient to normal good health indicates very conclusively that the spleen is the instrument which produces the pathological hæmolysis. Despite the incompleteness, therefore, of our knowledge of the pathogenesis, clinical experience has so overwhelmingly demonstrated the value of the treatment, that there is no doubt whatever that for patients in whom the diagnosis is clear, splenectomy should be confidently undertaken.

The two patients whom we have to report are particularly interesting in that they are sisters, daughters of a man who died at the age of fifty-four years of a profound anæmia and marked jaundice. The disease in his case had developed suddenly about four years before, and there had been several distinct periods of remission followed by acute exacerbations,

in one of which he finally succumbed. The diagnosis made without blood-examination was pernicious anæmia, but our patients, who remember their father's illness distinctly, state that his case resembled theirs in every clinical detail, and both they and we are convinced that he died of typical hæmolytic icterus.

We saw the first of the sisters, Mrs. W., in January, 1917, at the age of thirty-nine years. She had had perfect health until two years previously, when she began to lose her appetite and to diminish in weight and strength. For a year she was able to continue her work on the farm, but she ultimately became so weak and miserable that she was forced to give it up. In April, 1916, the symptoms suddenly become more marked with the addition of constipation and jaundice. During the summer she improved considerably, and the jaundice lessened, but during the last two months of 1916 she underwent another exacerbation of symptoms with the development of profound weakness and dyspnoea. At this time she became aware of moderate pain in the left side of the abdomen, and this led to the discovery of a large mass in the left hypochondrium. During the examination she was seen by several consultants, who found her exceedingly pale and jaundiced. With the jaundice was none of the other signs of biliary obstruction, such as itching of the skin and clay-coloured stools. The spleen was markedly enlarged (a hand's breadth below the costal margin) and the liver slightly so. The urine was acid, muddy brown in color, and full of urates, but there was no bile-pigment present. Examination of the blood showed approximately 2,000,000 red cells, hæmoglobin 30 per cent, with a colour index of .75. There was considerable poikilocytosis, a good many normoblasts, and some megaloblasts. The white count showed 4,000 leucocytes. Her temperature was ranging daily from 99.3° to 101°, and she suffered from frequent sweats. Her weight was 98 pounds, whereas her normal weight was about 120 pounds. A provisional diagnosis of some form of splenic anæmia was made and splenectomy advised.

As a preparatory measure to operation, 800 c.c. of blood was transfused from a brother on February 4th, 1917, and a week later on February 13th the spleen was removed. It was

markedly enlarged, weighing 850 grammes, deeply congested, and without any signs of adhesions or other evidences of fibrotic change. The sections showed a condition of simple congestion and hyperplasia of the spleen pulp. The liver, gall-bladder and bile-ducts appeared normal.

A few days after her operation she was given another 600 c.c. of blood and from that time forward made an uneventful recovery. The jaundice disappeared in the course of three weeks and has never returned. Her strength and weight rapidly improved and in the course of eight weeks she returned to her work on the farm. Six months after her operation she felt quite normal again and had gained twenty-five pounds in weight. We saw her in June, 1920, and found her in excellent health, weighing 132 pounds, with a good appetite, looking young for her years (44) and without a sign of jaundice. She was running a large farm without the assistance of a maid, working all day and seldom tired. The blood-picture was as follows:

Red blood-cells,	4,000,000
Hæmoglobin,	80% (Sahli)
Colour index,	1.2
White blood-count,	12400
Polymorphonuclears,	62%
Small lymphocytes,	29%
Large lymphocytes,	4%
Eosinophiles,	5%

The red blood-cells were regular in shape and size but they all appeared to be at least 1/3 larger than the normal cells with which they were compared. No nucleated reds or other abnormal cells.

Auto-agglutination test negative.	
Vital stain—no reticulated or skein cells.	
Resistance to hypotonic salt solution, (cells both washed and unwashed.)	
Partial hæmolysis at3%
Complete hæmolysis at2%
No hæmolysis at35%

This indicates a decided increase in the resistance of the red cells over normal to hypotonic salt solution, but unfortunately it is impossible to make a comparison with the condition previous to operation as no fragility test was made at that time.

In the spring of 1921 she consulted her family doctor with symptoms of palpitation, tremulousness and general weakness. He made a diagnosis of toxic goitre based on tremor, rapid pulse (130) and fullness of the neck. There was

no exophthalmos. These symptoms continued till early in 1922 when she went into hospital for three months and received x-ray treatment. She improved rapidly under treatment and has been comparatively well ever since.

We saw her again in March, 1923. She looked well, weighed 140 lbs, showed no tremor or tachycardia and was of excellent colour. A blood-count showed 5,000,000 red cells, hæmoglobin 100 per cent (corrected Sahli) and white cells 12,000. The red cells appeared in every way normal.

In the autumn of 1923 she was presented at the meeting of the American Interurban Surgical Society in Toronto and the examination at that time justified her classification as a cure.

Since then we have not seen her but we have a letter dated January 4th, 1926, in which she states that as far as her old anæmia and jaundice are concerned she is splendid, although she complains of some symptoms which may be attributed to the menopause. She is still carrying on at her work on the farm.

Case 2. Mrs. B., aged forty-nine, sister of Case No. 1.; first seen by us March 1, 1923

Until the spring of 1920 she had been in perfect health. At that time she began to feel unusually tired with ordinary work and coincidentally she developed jaundice. She consulted her physician in April, 1920, about a month after the onset of symptoms. He observed the jaundice at once, and also noted the high coloured urine and normal looking stool. During the summer she lost considerable weight, ran a fever up to 101 and felt generally miserable. About this time she was visited by her sister, who at once saw in her a repetition of her own case. During the autumn and winter she improved decidedly although her jaundice persisted. In the following spring, 1921, she had a slight exacerbation which was not alarming, and improved again during the following summer and winter. In the spring of 1922, however, she went rapidly down hill, becoming breathless and subject to nausea and vomiting. Her jaundice became very marked, and the urine deeply yellow. In June 1922 she was sent into hospital and here it was found that the spleen was much enlarged. Blood-examination at that time showed a profound anæmia with hæmoglobin under 25 per cent. She was transfused

by the citrate method, 400 c.c. and during the summer received four more transfusions at intervals of two weeks. A remission of symptoms then set in, and in many ways she improved. Her appetite returned, the spleen diminished considerably in size, the liver, which was enlarged a year previously, receded and the jaundice became less marked. Her general weakness continued, however, and she was unable to return to her work. She was under the impression for some time past that she was on the verge of another acute exacerbation, and this led to her coming to Toronto for treatment similar to her sister's.

Physical examination showed the following points of interest:

1. Jaundice.—A ruddy jaundice which has never been associated with itching.

2. Abdomen.—Spleen palpable, a couple of finger breadths below the costal margin. Liver not enlarged. Abdomen full, but no free fluid present. Clinical tests: red cells 3,850,000—no abnormal cells. Some variation in the size of the cells. No skein cells shown by vital stain. hæmoglobin 85-90% (corrected Sahli). White cells 6,700. Differential—polymorphs 55%, lymphocytes 42%, endothelial cells 1%, eosinophiles 2%. Auto-agglutination test on blood; positive; Wassermann, negative. Urine, dark amber, clear. Albumen and sugar absent. Bile absent. Urobilin test strongly positive. Faeces brown in colour. Fragility test, with both washed and unwashed cells; in patient's blood, hæmolysis began at 0.4%; in control's hæmolysis began at 0.45%; that is to say, the resistance of the red cells to hypotonic salt solution was increased rather than diminished.

From the history and examinations, a clear diagnosis of acquired hæmolytic icterus was made. In only one detail did she differ from the usual clinical picture of the disease, namely in the fact that there was no diminution of the resistance of the red cells to hypotonic salt solution. It may be that if the blood had been examined during a crisis of deglobulization, it would have shown increased fragility. On the other hand this case is not unique in showing absence of this convincing test, as several cases have been recorded in which it was absent.

On March 8, 1923 the spleen was removed. The gall-bladder and bile-duets were normal. There was no free fluid in the abdomen. The

liver was slightly enlarged and here and there were patches of sclerosis. A small piece of one of these was removed for section.

The spleen weighed 375 grammes and showed nothing abnormal beyond congestion. The piece of liver showed a moderate portal cirrhosis.

Following the operation the patient did extraordinarily well. She had no shock, no discomfort and no complications of any kind. Twenty-four hours later there was a distinct fading of the jaundice and at the end of five days it had completely disappeared. On March 15th the urobilin in the urine had diminished to a trace and on the 18th had disappeared.

She left the hospital on April 1st and we did not see her again till April 24th. During this period she made remarkable improvement. There were no signs of jaundice and the former yellow colour had been replaced by a clear healthy complexion. She had a general feeling of well-being which she had not had for years. The blood examination showed the usual physiological reaction which follows splenectomy, namely a moderate anæmia and a leucocytosis, red cells 2,500,000, white cells 10,500, hæmoglobin 60%, colour index 1.2. No abnormal cells could be seen but there was a little irregularity. The fragility test showed no hæmolysis at 0.45% salt solution and commencing hæmolysis at 0.4%. This was exactly the same reaction as before operation. No urobilin could be found in the urine.

The final examination was made on Sept. 1, 1923. By this time she had returned, as far as she or we could tell, to her normal good health. She had gained ten pounds in weight, had lost all evidence of anæmia and had acquired a ruddy complexion. She had lost her former breathlessness and was able to work continuously. The blood-examination was as follows: red cells 4,400,000, white cells 11,500,

hæmoglobin (corrected Sahli) 118 per cent. One or two nucleated red cells encountered in counting 200 white cells. The red cells were regular in size and shape but appeared to be a little larger than normal. Fragility-hæmolysis begins at 0.45 per cent, the same as control. Auto-agglutination negative.

Since Sept., 1923, we have not seen the patient as she lives in the far west but from time to time she writes that she is in perfect health. A few days ago a letter arrived in which she describes herself as feeling as well as she ever did in her life without sign of anæmia or jaundice.

A review of these two cases shows two women, one of thirty-seven years of age and the other forty-nine, daughters of a man who died of a similar condition at the age of fifty-four, suddenly attacked by a disease characterized by profound anæmia, acholuric jaundice and enlargement of the spleen. In both cases the disease progressed with periods of remission and definite acute exacerbations. In the younger, the spleen was removed in the midst of a crisis of deglobulization and in the elder, in a period of remission. Both made astonishing recoveries and have returned to normal good health, the former over a period of nine years and the latter, four years. Whether the cure is permanent or not, only the lapse of time can show, but the results of treatment, thus far, have amply demonstrated the value of splenectomy in this disease.

These two cases have been reported at length in order that they may be added to the rather recent literature of hæmolytic icterus and in order that attention may be drawn to the importance of accurately differentiating by the various diagnostic methods at our command, those distinct diseases, once grouped under the name of "Splenic Anæmia" for which splenectomy may be expected to accomplish a cure.

Bovine Tuberculosis.—The Royal Commission of 1911 had disproved Koch's statement that this form of tuberculosis was not a serious menace to man. In a recent investigation by Griffiths the bovine bacillus was found in 85 per cent of cases of gland tuberculosis in chil-

dren under five years of age; in bone and joint tuberculosis 30 per cent; in lupus 66 per cent; and in meningitis 66 per cent. These findings emphasize the urgent necessity for the pasteurization of milk.—*Lancet*, March 7, 1925.

SPLENECTOMY FOR PURPURA HÆMORRHAGICA

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INTRODUCTION

CERTAIN hæmorrhagic conditions having as a common feature the striking symptom of bleeding into the skin and from the mucous membranes, are grouped together under the diagnosis of purpura. The petechial hæmorrhages and ecchymoses which are common to all purpuras, are however, but symptoms of a fault in the mechanism of blood coagulation which may be due to one of several different causes. The group is therefore a heterogeneous one gathered together on the basis of a common symptomatology, without reference to the underlying and usually unknown cause.

Even on the basis of symptoms it has been possible to distinguish certain subgroups amongst the purpuras. Thus, we are accustomed to recognize as distinct types, Henoch's purpura, distinguished by hæmorrhages into the intestine, and peliosis rheumatica, distinguished by an accompanying arthritis. As long ago as 1887 Denys¹ first made an observation which distinguished a pathological basis for certain of the purpuras, when he noted, in a case of purpura which he had studied, a great deficiency in the blood platelets. In 1889 Hayem² confirmed this finding and reported a similar condition in several other cases of the same disease. This feature seems to have aroused little comment until Frank³ reported the results of his investigations, viz., that marked diminution in the number of platelets was a constant feature in that type of purpura described clinically as Werlhof's disease or morbus maculosa. He believed the lack of platelets to be due to deficient production of them on the part of their parent cells, the megakaryocytes of the bone marrow, and regarded the disease as a form of aplastic anæmia. He considered the deficiency in platelets to be the cause of the hæmorrhagic tendency, and proposed for the condition, the term essential thrombopenia. This loose term, since it may mean either deficiency in platelets (thrombocytes) or in

thrombin, has been replaced by the more accurate designation, thrombocytopenia, proposed by Eppinger.

Numerous investigations since Frank's paper have confirmed the fact that many cases of purpura, though not all, are associated with this great diminution in the number of platelets in the blood. On this basis it is possible to classify the purpuras into two groups, dependent upon whether the platelets are present in normal or diminished numbers (See Table I.)

TABLE I
CLASSIFICATION OF PURPURAS

<i>Thrombocytopenic Group</i>	<i>Non-Thrombocytopenic Group</i>
<i>Platelets diminished in numbers</i>	<i>Platelets normal in numbers</i>
1. Symptomatic purpuras	1. Henoch's purpura
(a) Due to infections:	2. Peliosis rheumatica
Streptococcic	
Staphylococcic	
Pneumococcic	
(b) Due to exanthemata	
Hæmorrhagic smallpox	
(c) Hæmorrhagic forms of diseases of the hæmatopoietic organs	
Leucæmia	
Pernicious anæmia	
(d) Due to poisons:	
Benzol	
2. Idiopathic purpura	
Werlhof's disease	

The interest of the present paper lies with the thrombocytopenic group of purpuras. As knowledge concerning them has accumulated, it has become evident that, while marked diminution of the platelets is a feature common to the whole group, there is more than one factor producing the loss of platelets. Certain intense bacterial infections by streptococci and pneumococci are sometimes accompanied by thrombocytopenia and hæmorrhages. The hæmorrhagic form of small pox (Ikeda⁴) is also characterized by marked thrombocytopenia. In the hæmorrhagic forms of diseases of the hæmatopoietic system (leukæmia, aplastic anæmia and pernicious anæmia,) there is also a lack of platelets in the blood, presumably because the megakaryocytes of the bone marrow are involved together with the other blood form-

ing elements. Certain poisons, notably benzol¹¹ also produce thrombocytopenia and hæmorrhages. Apart from these conditions, in which the thrombocytopenia may be regarded as symptomatic of some grave underlying disease, there exists a certain group of cases unassociated with any other pathological condition, in which purpura and thrombocytopenia are the sole pathological symptoms. It is to this subgroup, known clinically as idiopathic purpura, Werlhof's disease or morbus maculosa, that Frank applied the term essential thrombopenia.

In 1916 Kaznelson⁵ made the observation that of three cases of the essential type of thrombocytopenia, two had enlarged spleens. By a happy chance he conceived the idea that the enlarged spleen was evidence of the fact that this organ was the cause of the diminution in number of platelets, and that removal of the spleen would cure the disease. He carried out his idea by removing the spleen from a woman, who, for ten years, had suffered from menorrhagia and epistaxis of such severity as to endanger her life. Before operation the platelets numbered 3,000 per cubic millimeter. Following splenectomy they rose at once to 500,000, and coincident with this the hæmorrhages ceased. The dramatic cure thus obtained has been permanent. Two years later he⁶ reports her restoration to normal health to have been maintained.

Kaznelson's case with its striking cure focussed attention upon the existence of essential thrombocytopenia, and the possibility of its cure by surgical measures. A considerable number of cases treated by splenectomy have since been reported, and the number is growing rapidly.

Clinical symptoms of essential thrombocytopenic purpura.—An outline of the clinical picture of this disease may not be out of place. Essential thrombocytopenic purpura occurs most frequently in female children. It is not hereditary, though it is occasionally present at birth. Its onset frequently is associated with an infection. This occurs sufficiently often to impress one with the possibility that infection may be the primary cause of the change which leads to excessive platelet destruction. The outstanding symptoms are hæmorrhages into the skin and from the mucous membranes. The cutaneous hæmorrhages vary in size from

pinpoint petechiæ to the largest ecchymoses. They are most numerous in the dependent parts, or in those parts where, for any reason, the capillary pressure is raised. Hæmorrhage from the mucous membranes commonly gives rise to epistaxis, bleeding from the gums, and less commonly to hæmatemesis, and in females to menorrhagia. The cutaneous hæmorrhages are not always present, and as knowledge concerning the disease accumulates, it becomes evident that many bizarre forms of hæmorrhagic diathesis are in reality cases of essential thrombocytopenia. The literature contains reports of cases of hæmorrhage in the newborn, intracranial hæmorrhage, menorrhagia of puberty and of the menopause, and persistent epistaxis, all associated with thrombocytopenia, and cured by splenectomy in such cases as this measure has been used. The resistance of the capillary walls is very low, and in consequence the most trivial injury results in bleeding into the skin. For the same reason constriction of the veins of the arm by a tourniquet, without completely shutting off the arteries, so that venous engorgement of the arm and increased capillary pressure are produced, results in the formation of a crop of petechiæ below the tourniquet in two or three minutes. This is the capillary resistance test of Hess⁷. Acute and chronic forms of the disease occur. The former are of abrupt onset, and run a fulminating course, often fatal in one or two days. These acute cases, however, may recover completely, or may pass over into the chronic form. There is some question as to whether many of the acute cases, particularly the fatal ones, are really examples of essential thrombocytopenic purpura. Evidence is accumulating which points to their being symptomatic purpuras due to intense infections. They do not respond to splenectomy as do the chronic cases. The chronic form occurs in all degrees of severity, from that in which the tendency to hæmorrhage is merely an inconvenience, to that in which the constant and severe hæmorrhages reduce the patient to a state of chronic invalidism. The more severe forms are the commoner. They last for months or years, and usually end fatally. They may be intermittent in type. In seventy-five per cent of chronic cases the spleen is sufficiently enlarged to be palpated.

The blood changes are striking and characteristic. The platelets are reduced in numbers to a very low level. Normally they number 200,000 to 400,000 per cubic millimeter. In essential thrombocytopenic purpura they are always below 100,000, and usually below 50,000 per cubic millimeter. They may almost completely disappear from the circulation; counts as low as 1,000 per cubic millimeter being recorded. The tendency to hæmorrhages becomes very marked as the numbers fall below 80,000 per cubic millimeter, until with extremely low counts the most persistent hæmorrhage exists. The bleeding time, i.e. the time necessary for the spontaneous cessation of bleeding from diagnostic punctures, is greatly prolonged. Normally it is from two to three minutes. In this form of purpura it is prolonged to ten or fifteen minutes, or even longer. The length of the bleeding time, in the severe cases, is dependent in part upon the size of the puncture. The larger pinpricks will bleed indefinitely, stopping only when pressure or styptics are applied. Only the smaller pinpricks cease bleeding spontaneously, and then only after an abnormally long time. The blood, if drawn into a test tube, clots in the normal length of time, i.e. two to three minutes. This normal clotting time is in sharp contrast to the prolonged bleeding time, and a satisfactory explanation of it has not yet been given. It is believed that bleeding through ruptures in the capillary walls is normally stopped by plugs of agglutinated platelets, and that the paucity of platelets in this disease accounts for the delay in closure of the breach. On the other hand, the presence of even a few platelets in the blood withdrawn into a test tube is sufficient to initiate the process of coagulation in the normal length of time. The clot thus formed *in vitro*, while appearing in the normal time, is soft and easily broken. It contains little fibrin. It does not retract and extrude serum within a few hours as does a normal clot. Even after standing for days the clot from a severe case of thrombocytopenic purpura does not retract. Apart from a secondary anæmia, sometimes of severe degree, due to the hæmorrhages, there are no other characteristic blood changes.

To summarize, essential thrombocytopenic purpura is a disease characterized by:—1. A

hæmorrhagic tendency manifested by hæmorrhages into the skin and from the mucous membranes. 2. Diminution in the number of platelets. 3. Prolonged bleeding time. 4. Normal clotting time. 5. Failure of the clot to retract. 6. A positive capillary resistance test. 7. An enlarged spleen usually.

Pathogenesis.—A satisfactory explanation of the pathology of the condition has yet to be given. Frank originally regarded it as a form of aplastic anæmia affecting chiefly the megakaryocytes; the thrombocytopenia being due to a diminished production of platelets. Following the introduction of splenectomy he modified his view, believing that the enlarged and diseased spleen produced a toxin which had an inhibitory effect upon the megakaryocytes, resulting in diminished production of platelets. It is difficult to reconcile this view of the disease with the instant rise in platelet count which occurs after removal of the spleen. Within a few hours the count is materially increased, and within twenty-four hours the rise is great. Kaznelson's view is that the spleen normally destroys platelets, and that in this disease it has taken on an abnormally great destructive role. He felt that this view was confirmed not only by the rapid rise in platelets after splenectomy, but also by the fact that in his first case he found the splenic sinuses packed with platelets. This latter observation has not been confirmed by more recent writers. In nearly all the recorded cases the platelet count ultimately falls, and usually to a subnormal level, sometimes as low as it was before operation, though without recurrence of the hæmorrhagic symptoms. On the splenolytic theory it is difficult to explain this phenomenon. While the deficiency in platelets is the striking feature of the disease, there must also be some alteration in the capillary endothelium to permit such a sign as the positive capillary resistance test. The nature of this is completely unknown, as is also the reason for its disappearance after splenectomy.

Treatment.—Prior to the introduction of splenectomy for this disease, the treatment was extremely unsatisfactory. No drug or serum has the slightest influence upon the bleeding. Pressure is of some value; but the bleeding occurs in many situations (e.g. mouth) in which pressure is difficult to apply. The severe cases

therefore are pitiable. They bleed continuously and become extremely anæmic and weak. The accumulated blood in the nose and mouth becomes infected and gives rise to a foul smelling discharge. Transfusion is of definite, though temporary, value. It is the only measure short of splenectomy which will stop severe hæmorrhages. Its beneficial effect does not last more than a few days. Irradiation of the spleen by x-rays has been uncertain in its results, but ligation of the splenic artery (Lemaire and Debaisieux⁸) in at least one case in which the major operation of splenectomy was thought inadvisable because of the condition of the patient, has produced the same result as splenectomy.

Since Kaznelson reported his case in 1917, a considerable number of patients suffering from essential thrombocytopenic purpura have been treated by splenectomy. In May 1925 Giffin and Holloway¹⁰ summarized the reports of twenty-eight cases which had appeared in the literature to that date. Since his paper I have been able to find records of eighteen further cases^{13 to 22} making in all forty-six cases. It is probable that there are other cases reported in continental literature to which I have not had access.*

The results of splenectomy have been very well analysed by Giffin and Holloway¹⁰ and Vincent²². In the great majority of cases the operation has resulted in a dramatic disappearance of the hæmorrhagic symptoms. Making every allowance for the probability that failures of this treatment have been incompletely reported, there can be no doubt that splenectomy is a marked advance in treatment. Five deaths are reported; two in which the operation was undertaken in acute cases, probably inadvisably, one from chloroform poisoning, one from a sub-phrenic abscess, and in one case the cause of death is not clearly defined.

In practically every case splenectomy is followed immediately by a marked rise in the platelet count to a normal or even super-normal level. The maximum height is reached in five to eight days, is maintained for about a week, and then slowly declines, until in the course of a few weeks it becomes stationary at a normal

or sub-normal level. Occasionally, though not usually, it falls as low as before operation. As a rule the platelet count after operation is higher than it was before, though often it is still below normal. Coincident with the rise in platelet count, the hæmorrhage ceases, and in the great majority of cases does not return with the subsequent fall in the platelet count. A few patients have had recurrences of hæmorrhage when this stage is reached, but such hæmorrhages are of mild degree and easily controlled, in contrast to the condition which existed before splenectomy. The prolonged bleeding time, capillary resistance test, and clot retraction also return to normal following splenectomy, though not with the same certainty and constancy as does the hæmorrhagic tendency. In those patients in which recurrence of symptoms has taken place, infection appears definitely to play a part. The majority of such recurrences have followed immediately upon an infection of the respiratory tract.

The obscurity of the primary changes underlying the disease precludes an accurate interpretation of the changes which follow splenectomy. The general belief is that the spleen normally destroys effete platelets, and that in this disease it possesses an abnormally great thrombocytolytic action. In an attempt to maintain the normal balance the production of platelets is greatly increased, and this explains the presence of the large and immature forms of platelets which have been observed in the disease. Removal of the spleen permits production rapidly to overtake destruction, and the platelet count rises in consequence. After the removal of the spleen it is believed that other elements of the reticulo-endothelial system take on the function of destroying platelets, and as their activity increases the platelet count falls, until a balance again is reached at a lower level. Bedson²³ is of the opinion, based upon his work in experimental purpura, ingeniously produced, that splenectomy cannot result in a permanent cure of essential thrombocytopenic purpura. All such theoretical conclusions, however, are based upon the variations in numbers of platelets. It seems certain that something more than paucity of platelets is concerned in the production of the disease, as is evidenced by the persistence of the cure which follows splenectomy, in spite of the low level of the plat-

*Since this paper was written, A. O. Whipple, (S. G. & O. vol. xlii, March, 1926, p. 329), has published an excellent summary of all the reported cases. He has been able to collect eighty-one cases.

clet count which occasionally occurs. Nothing is known, either, as to the nature of the change in the capillary walls which permits the petechial hæmorrhages so readily. In the present state of our knowledge the only conclusion which can be drawn in respect to treatment is the empiric fact that splenectomy will practically always produce a symptomatic cure.

It is as yet too early to draw definite conclusions as to the permanency of the cures so obtained. Vincent²² reviews the earliest cases, three patients of Kaznelson's, who were well at the end of six and seven years. On this continent the first patient was operated upon in 1922 by Bowen¹². Such reports as are available indicate that the symptomatic cure obtained by splenectomy, in most cases, has been maintained.

Case Report.—To the cases already reported I am adding the following case history:

D. K., female, age eleven years, was admitted to the Hospital for Sick Children for treatment on Oct. 1, 1925. She had been suffering from endocarditis since 1920. In October, 1922 her tonsils and adenoids were removed as part of the treatment of her heart condition. This was followed by a severe hæmorrhage, only controlled by transfusion. The mother had noticed that she always bruised easily, and some time prior to the tonsillectomy, extraction of a tooth had been complicated by hæmorrhage. In September,

1925, a number of petechial hæmorrhages appeared on her body. These increased in number and extent up to the time of her admission to hospital on October 1, 1925. They were particularly numerous on the legs. Immediately prior to her admission it was noticed that she bruised with much greater ease than formerly. She had had a blood-stained nasal discharge for a month prior to admission.

Examination on admission, Oct. 1, 1925, revealed her to be a pale, sick child. Temperature 100.2°, pulse 108. The skin was filled with hæmorrhages which were much more numerous on the lower extremities than elsewhere. They varied in size from a pinpoint to very large subcutaneous bruises. There were submucous hæmorrhages into the lips, tongue, tonsil and palate. There was bleeding from the left nostril. The spleen was palpable half an inch below the costal margin. The capillary resistance test of Hess produced a numerous crop of petechiæ in one minute. Blood examination showed R.B.C. 3,880,000, Hb 85%, W.B.C. 15,000, platelets 12,500, bleeding time 25 min. (Fig. 1) clotting time 4 min. The blood withdrawn into a test tube clotted readily, but the clot thus formed did not retract even after several days (Fig. 2.) The diagnosis of essential thrombocytopenic purpura was therefore clear.

On Oct. 5, 1925 the nasal hæmorrhage became very severe so that by the morning of Oct. 6, 1925 the child was exsanguinated and pulseless. The nose was packed and the patient transfused with 500 c.c. of blood. This stopped the bleeding temporarily and produced a distinct improvement. On Oct. 10, 1925, the nasal bleeding recommenced, and from that time until the spleen was removed on Oct. 30, 1925, nasal hæmorrhage was a continuous and distressing feature. It was necessary to keep a nasal tampon in place continuously. The blood from the nasal hæmorrhage became infected and resulted in an extremely foul smelling discharge. Fresh crops of petechiæ appeared each day, though the numbers were always less than before transfusion. The blood findings remained practically

TABLE II
BLOOD FINDINGS IN CASE REPORTED

Date	Platelets	R.B.C.	W.B.C.	Hbn.	Clotting Time	Bleeding Time	Clot Retraction	Cap. Resist. Test
Oct. 1, 1925..	12,500	3,880,000	15,000	85%	4 m.	25 min. +	Nil	+
" 3, 1925..	12,500							
" 5, 1925..					4½ m.	30 min.		
" 6, 1925..	Transfusion 500 c.c.							
" 8, 1925..		3,260,000	12,700	75%	4 m.	12 min.		
" 9, 1925..	16,600							
" 16, 1925..	19,300							
" 27, 1925..	31,000					14 min.		
" 29, 1925..	21,000				5 m.	30 min. +	Nil	
" 30, 1925..	Splenectomy and Transfusion 580 c.c.							
" 30, 1925..	65,000							
" 31, 1925..	144,000							
Nov. 1, 1925..	342,000							
" 2, 1925..	595,000					2 min.	+	neg.
" 3, 1925..	800,000							
" 4, 1925..	960,000				4 m.	1 min.	+	neg.
" 5, 1925..	1,010,000							
" 6, 1925..	1,024,000							
" 8, 1925..	840,000							
" 9, 1925..	1,028,000							
" 10, 1925..	898,000							
" 13, 1925..	914,000							
" 15, 1925..	1,040,000				4 m.	4½ min.		
" 17, 1925..	828,000							
" 19, 1925..	780,000							
" 22, 1925..	890,000							
" 27, 1925..	756,000	4,252,000						
Dec. 5, 1925..	603,000							
Jan. 25, 1926..	504,000	5,120,000		75%	5 m.	6 min.	+	neg.

unchanged (Table II). Platelets ranged from 12,000 to 20,000. They were only slightly increased by transfusion. The bleeding time was greatly prolonged. From the most minute pinprick it was possible to make bleeding continue for about 30 min. (Fig. 1), while from a larger pinprick such as that which is ordinarily used to obtain blood for blood counts, there was no tendency whatever to spontaneous cessation. The clotting time was normal. The clot showed no tendency to retraction even after long periods of time. The capillary resistance test was always positive. The spleen became much larger during the month she was under observation.

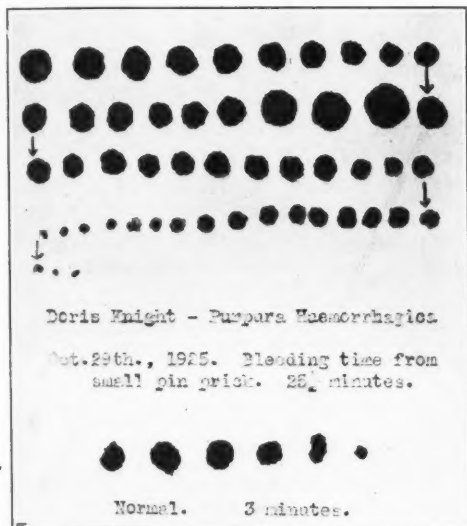


FIG. 1.—Graphic record of the bleeding time by Duke's method. Blood from a small pin prick was absorbed on a piece of blotting paper every thirty seconds. Every second drop of blood represents therefore one minute of bleeding time.

On October 30, 1925, splenectomy was performed through a left-sided Bevan incision; after a preliminary transfusion of 580 c.c. of blood. Moderate hemorrhage was encountered, but this gave rise to no unusual difficulty. The splenic pedicle was short, and this somewhat prolonged the operation, since it precluded delivery of the spleen outside the abdomen. After removal of the spleen the pedicle was oversewn and the denuded splenic bed covered with peritoneum.

She made an uneventful recovery from the operation. The wound healed by first intention. The nasal bleeding ceased immediately after the operation, and has not since recurred. The petechial hemorrhages faded and no new crops have appeared. The platelet count rose immediately (Fig. 3). On the afternoon of the day of the operation it was 61,000. The following day it was 144,000. By the eight post-operative day it had reached its maximum of 1,028,000. It remained at this level for about a week and then slowly declined. At the time of writing, three months after operation, it is 500,000. Three days after the operation the bleeding time was two minutes. The clot retracted well (Fig. 2) and the capillary resistance test was negative. These findings have persisted to the present. The improvement in her general health has been very remarkable. From an anæmic, bleeding, septic invalid, she has been changed to a normal girl of good colour and of normal activity. There has been no recurrence of hemorrhages from the mucous membranes or into the skin.

The spleen was examined by Dr. I.H. Erb, Pathologist to the Hospital for Sick Children, who reports upon it as follows:

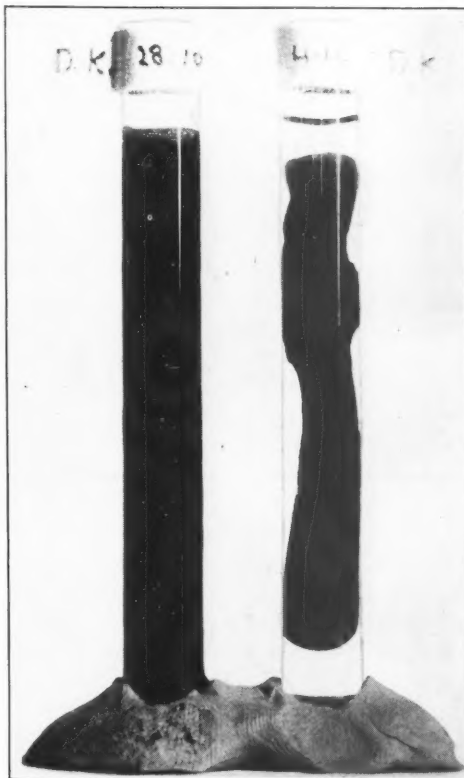


FIG. 2.—Change in the nature of the clot following splenectomy. The left hand specimen was obtained two days prior to splenectomy and six days later when the photograph was taken no retraction of the clot had occurred. The right hand specimen was obtained four days after splenectomy. The clot retracted in the manner shown in four hours.

The removed spleen weighed 164 gms. and measured 11 x 8 x 3.5 cms. The consistency was normal and the colour a purplish red. The organ was injected with 10 per cent formalin through tributaries of the splenic vein. After fixation, section of the spleen showed a healthy surface of dark purplish red colour, with medium sized Malpighian corpuscles present in approximately normal numbers. There was no evidence of increase in the connective tissue. Microscopically, under low power, the splenic tissue appeared normal. The capsule and trabeculae were not thickened, and the Malpighian corpuscles were normal. Many of the vessels were empty due to the formalin injection; others contained blood. Under high power, the various structures also appeared normal, except that in the splenic pulp there were seen quite a number of cells with eosinophilic granules. The majority of these had polymorphous nuclei, but an occasional cell was seen in which the nucleus was almost round. A number of sections were stained with Wright's platelet stain, but no platelets could be demonstrated. Cultures of the splenic pulp taken before fixation remained sterile.

Comment.—The case reported was one of essential thrombocytopenic purpura of severe de-

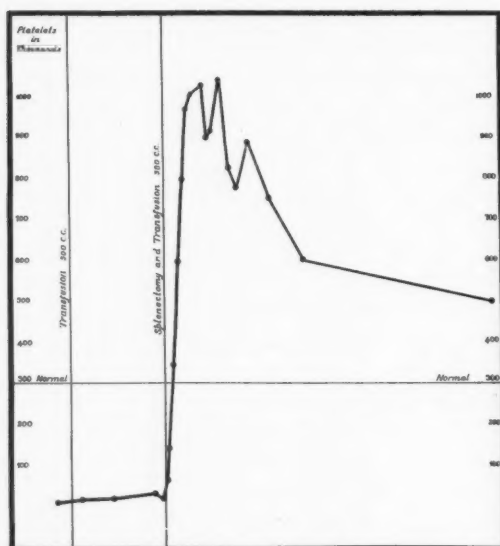


FIG. 3.—Graph of the variations in the platelet count for one month preceding and for three months following splenectomy.

gree. Transfusion was of some palliative value, but splenectomy produced an immediate cure. The clinical picture and the result from splenectomy are in accord with previously reported cases.

Conclusions

1. Essential thrombocytopenic purpura may be isolated from the remaining purpuras by the distinctive clinical findings. 1. Low platelet count. 2. Prolonged bleeding time with normal coagulation time. 3. Positive capillary resistance test. 4. Failure of the clot to retract. 5. An enlarged spleen usually.

2. Infection plays a prominent part in the production of the obscure pathological change which gives rise to the disease.

3. The most important, though not only factor causing the hæmorrhagic condition is the thrombocytopenia.

4. Splenectomy produces a symptomatic cure in a dramatic fashion.

It is a pleasure to acknowledge my indebtedness to the medical service of the Hospital for Sick Children, and in particular to Dr. Geo. E. Smith, for the opportunity of treating this case; to Dr. C. H. Watson for his painstaking care in making the numerous platelet counts; and to Dr. I. H. Erb for the pathological report.

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The Rotary Club of Vancouver has for years been interested in the Tuberculosis Campaign. They formed a Rotary sub-committee to administer Club funds in the interests of returned sanatoria cases. Immediately they are notified of a man or woman returning to Vancouver, they approach their members and friends, obtain part-time employment—two hours in the morning and two hours in the afternoon—increasing as the doctor approves. The employer and employees are sympathetic and do not shun the ex-sufferer. The committee finds support for the home. The worker goes at noon

to the institute, has temperature, pulse and weight recorded by a nurse, is seen by a doctor if necessary, has a hot meal provided for 35c. and then absolutely relaxes for an hour by lying down in bed on one of the porches before returning to work. This supervision, sympathy and financial re-establishment, together with the hour's rest just make the difference daily between success and failure. The smallest community or committee could easily improvise the requirements for this necessary work to save a father for his boy.

BLOOD REGENERATION*

BY NATHAN B. EDDY, M.D., AND ARDREY W. DOWNS, M.A., M.D., D.Sc.

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A COMPLETE discussion of blood regeneration probably should include a consideration of the means of restoration of blood volume, that is, of the watery or inorganic parts of the blood, the replacement of blood proteins, and regeneration of hæmoglobin and blood corpuscles, the red blood corpuscles especially. It might very properly include also a consideration of the various types of anæmia in which blood regeneration is involved. However, we propose to describe briefly the spontaneous regeneration of red blood corpuscles and hæmoglobin in simple anæmia only, and to give consideration to some of the means at our disposal for speeding up this process.

A very extensive and very carefully controlled investigation of this type of blood regeneration has been carried on through the past ten or twelve years by Whipple and his collaborators. Their experiments have been performed upon dogs in two series. In the first series¹ each dog was bled one-fourth of its blood volume and two days later was again bled a like amount. This produced a simple acute anæmia and the rate of recovery as affected by various conditions was studied. In this study they observed the weight and condition of the animal and repeatedly determined total blood volume, corpuscle and plasma volumes, hæmoglobin and corpuscle content of the blood as indices of the rate of recovery.

On a mixed diet of bones, bread, cooked meat, potato and table scraps the dogs recovered from such an anæmia in four to seven weeks. Even during fasting some blood regeneration occurred, more indeed than when the dogs were fed sugar alone. This could only indicate the existence of a reserve of material within the organism from which hæmoglobin and corpuscles could be regenerated in the absence of building material in the diet. This and other evidence showed a very high degree of conservation by the organ-

ism of such protein split products as are suitable for rebuilding red cells and hæmoglobin. At the same time, there was no evidence that the organism ever breaks down tissue protein simply to supply material for blood regeneration. The store of reserve material is held principally in the liver, but probably also in the spleen, bone marrow and skeletal muscle. The liver is also concerned in the conservation of the protein split products. The authors deduce further from the sugar feeding experiments that the sparing of protein by carbohydrate is two-fold; prevention of breaking down of tissue protein and conservation of the split protein products when breakdown does occur.

They found that on a diet consisting only of bread and milk in abundance, blood regeneration was very slow. Recovery from the anæmia might be complete in six weeks or might take longer. When given in moderate quantity this diet will rarely permit of complete blood regeneration, and on an amount of bread and milk just sufficient to keep the dogs in normal health and activity, hæmoglobin and corpuscles remained permanently subnormal. An amount of regeneration just equal to the daily wear and tear took place, and this they call the maintenance factor.

To this basal diet of bread and milk in limited amounts various substances were added to determine their accelerating effect upon blood regeneration. Of these substances cooked beef liver was the most efficient, always accelerating hæmoglobin and red cell formation, even under the most adverse experimental conditions. It apparently did so because it contained necessary material, the appropriate building stones, for blood manufacture. An aqueous extract of liver was relatively inert. Lean beef and beef heart were in some cases almost as effective as beef liver for promoting blood regeneration, but the favourable reaction was not so invariable in its occurrence or degree.

Iron, either as Bland's pill by mouth or as

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ferric citrate subcutaneously, was without effect. Arsenic, as sodium cacodylate or Fowler's solution, was also ineffectual.

Hæmoglobin by mouth, subcutaneously, or intraperitoneally always speeded up regeneration of the blood cells and hæmoglobin. However, it was no more effective than beef liver and, cost, convenience of administration, etc., considered it possessed no particular advantage over lean beef.

The second series of experiments performed by Whipple and Robschitz² was designed to test even more rigidly the efficacy of various factors in regard to blood regeneration. Apparently the reasoning which prompted the experimental procedure was as follows: Wear and tear upon hæmoglobin and red blood corpuscles is probably approximately constant from day to day in the normal animal and if hæmoglobin content and corpuscles are remaining constant regeneration must be just equal to wear and tear; if hæmoglobin is increasing the regeneration must be surpassing wear and tear by the amount of the increase. This wear and tear was estimated as averaging 11.5 grams of hæmoglobin per week for a dog weighing 10 kilograms, whose blood volume was 500-600 c.c., and containing 17-20 grams of hæmoglobin per 100 c.c. of blood.

In these experiments the dogs were bled in moderate amount at one or two day intervals, until the hæmoglobin content was reduced to 50 per cent or 40 per cent of its normal level. Keeping the hæmoglobin at this low level would assure a constant maximal stimulus for blood regeneration and, sooner or later, a complete exhaustion of reserve materials for hæmoglobin and corpuscle building. The same determinations were made week by week as in the first series of experiments and the dogs were bled sufficiently to keep the hæmoglobin at the low level of 40-50 per cent of the normal amount. The hæmoglobin removed in these subsequent bleedings was accurately determined and must quantitatively represent the amount produced in excess of the maintenance factor.

After many trials it was found that a specially prepared bread composed of wheat flour, potato starch, bran, sugar, cod liver oil, canned tomatoes, canned salmon, yeast, salt and water (protein, 10.0 per cent; fat, 6.5 per cent; carbohydrate, 83.0 per cent) sufficed in all respects to keep the dogs in a normal healthy condition and yet hæmoglobin regeneration in most cases

just equalled that lost by wear and tear. With this established, the procedure was to feed this basal diet to the anæmic dog for two weeks, to feed during the next two weeks the basal diet plus some added factor and to feed during the next two weeks the basal diet again. A great number of dietary factors were studied as well as the remedies commonly recommended in the treatment of anæmia.

Again cooked beef liver was the most efficient dietary factor studied. It not only accelerated hæmoglobin regeneration markedly during the two weeks that it was fed, but the rate of regeneration continued to be accelerated during the following week. Evidently on a favourable diet the organism very quickly stored up reserves for hæmoglobin manufacture and quickly used up the reserve when the diet was unfavourable again.

Among the other factors studied by addition to the basal diet were lean beef, beef heart, iron, arsenic, germanium dioxide, various green vegetables and fruits. Lean beef and beef heart were less favourable for regeneration than in the first series of experiments, sometimes failing to have an effect. Arsenic and germanium dioxide were inert. Iron was distinctly favourable. It is to be borne in mind that the severity and long continuance of the anæmia had exhausted the reserve of iron in the animal's tissues as well as the reserve of organic material for hæmoglobin synthesis. The green vegetables and fruits were only moderately favourable; distinctly less so than in the earlier experiments in which reserves for blood building were not exhausted. Of those tried spinach and beet tops had the most influence. However close the chemical relationship between chlorophyll and hæmoglobin the animal does not seem able to make the necessary transformation to any great extent.

The outstanding features of this investigation are: Proof of the importance of dietary factors in blood regeneration; proof of the ability to control the rate of hæmoglobin and red cell production by diet; the apparent ineffectiveness of arsenic and germanium dioxide as hæmatopoietic stimulants; and the effectiveness of iron, as great in one form as in another, only when the iron reserve in the organism has been exhausted.

Many functions have been attributed to the

spleen and most of them in some fashion are related to the life cycle of the erythrocyte. At least one function, we think, can be said to have been proven. Robertson and Rous³ in 1917 demonstrated that the old red blood corpuscles undergo fragmentation in all parts of the blood stream and that this corpuscular debris is removed from the circulation mainly by the spleen, assisted by the bone marrow, liver and lymph nodes. In the absence of the spleen these other organs become capable of taking over the task completely.

Nearly five years ago we suggested, "That the splenic cells elaborate this material producing thereby an internal secretion, which was a component of the erythrocyte either stroma or pigment portion; that this internal secretion reduces the resistance of all the red blood corpuscles, the effect amounting to actual destruction of the older cells; and, finally, that this internal secretion, possibly after modification by the liver, stimulates the erythrogenic function of the bone marrow and is used up in the manufacture of new corpuscles."⁴ In the light of Whipple's work we might say that the spleen conserves one, or some, of the building stones for hæmoglobin and red corpuscle construction and passes them on to the bone marrow by the way of the liver. The ultimate purpose of the splenic function is to maintain the corpuscles in circulation at the acme of functional efficiency. This hypothesis is based upon the observations of Robertson and Rous, referred to above, upon our own work⁵ and that of others^{6,7} dealing with the effect of administration of splenic extracts and the changes which follow splenectomy.

Our own work has shown that the immediate effect of the subcutaneous injection of a splenic extract is a reduction in the number of circulating erythrocytes amounting to 20-30 per cent depending upon the dose, appearing in thirty to ninety minutes and lasting seventy to one hundred and sixty minutes. Later, the number of erythrocytes in circulation rises above normal and the count may remain above normal for a couple of days. Most of the other investigators have noted the later increase in the red corpuscles count only, because they have not looked for an effect within the first twelve hours after the injection. If the injection of splenic extract is repeated at daily intervals

the erythrocyte count rises gradually and remains fairly persistently above the normal level. We have seen large numbers of nucleated erythrocytes in the circulation after long continued daily injections of splenic extract⁸.

We believe that the initial decrease in the corpuscle count is a direct hæmolytic effect of the splenic extract. Such a hæmolytic action has been demonstrated *in vitro*⁹ although it seems that it is only the older less resistant cells which are thus hæmolyzed. Also we believe that the subsequent increase in the number of erythrocytes is due to stimulation of the bone marrow.

After splenectomy the erythrocyte count is decreased due to the absence of this stimulation or to the lack of building material, and the resistance of the remaining corpuscles is increased.

Our observations upon the effects of splenic extract have been confirmed by Leake¹⁰ both as to the immediate decrease in the erythrocyte count and the subsequent more persistent increase. In fact, he has adopted¹¹ our hypothesis of splenic function as if it were his own, and has lately recommended¹² the use of a splenic preparation in the treatment of anæmia.

Leake has also made an interesting contribution to the subject¹⁰. He found that an extract of red bone marrow had a slight hæmatopoietic effect, but if an extract of bone marrow and an extract of spleen were administered simultaneously the erythropoietic activity of both was enhanced and the initial decrease in the erythrocyte count, typical after splenic extract alone, was briefer or absent. He obtained identical results in kind by the use of fresh extracts of spleen and marrow administered subcutaneously, intravenously or by mouth, and by the feeding in capsule of dried powdered spleen and bone marrow. The dried powders were mixed in equal parts, and a dose of five grains of the mixture given once daily. Over a hundred cases of anæmia of various types have been treated with this combined powder. Leake reported the results in sixty-five of these cases. Of these 72 per cent were moderately or markedly improved in respect to the blood picture and other objective criteria, and the other 28 per cent showed slight or no improvement. "If the hæmoglobin percentage did not improve by five points, nor the erythrocyte

count by 250,000 cells, the case was classified as showing no improvement. If the haemoglobin percentage rose from ten to fifteen points and the erythrocyte count from 500,000 to 1,000,000 cells, the case was noted as moderately improved."

It might be mentioned in passing that Robscheit-Robbins and Whipple¹³ tried this combination of Leake's in one dog of their second series and obtained definite stimulation of haemoglobin formation.

In conclusion we wish to mention one other substance, an organic extract or internal secretion, which has not yet been tried clinically but which appears to possess definite haematopoietic activity. This substance is called secretin. For the past ten years we have been investigating the physiological activity of this substance, always having in mind the possibility of its clinical use, and searching constantly for the means of making a satisfactory preparation for this purpose.

When the hydrochloric acid of the gastric juice enters the small intestine it acts upon some substance in the mucosa, and as a result of this action a hormone is absorbed into the blood stream. This hormone stimulates the secretory activity of the pancreas and liver and undoubtedly effects other changes in the organism. The hormone is called secretin. If the mucosa of the excised small intestine is scraped off, and extracted in suitable manner with 0.4 per cent hydrochloric acid a preparation is obtained, evidently containing this hormone, which stimulates powerfully pancreatic and biliary secretion¹⁴ and which we have shown possesses other physiological properties^{15 & 16}. Perhaps the chief of these is its effect upon the number of red and white corpuscles in the circulating blood.

The subcutaneous injection of a small dose of a secretin preparation increases the number of both red and white corpuscles in circulation¹⁷. The increase attains its maximum in about sixty minutes and persists for sixty to ninety minutes. If the dose be repeated at hourly intervals the counts remain elevated above the normal for several hours after the last dose. We found that the administration of a daily dose of secretin subcutaneously over a period of eight weeks resulted in an increase in the erythrocyte count of 34 per cent and in

the leucocyte count of 37 per cent. At this time histological examination of the bone marrow showed very definite evidence of hyperplasia.

In another series of experiments¹⁸, rabbits were compelled to subsist on a diet consisting exclusively of broken polished rice. Three to six weeks of this diet reduced the red blood corpuscle count nearly 50 per cent and caused considerable loss of weight; that is, a definite dietary anaemia was produced. Then all of the animals were given a full mixed diet of oats and green vegetables and to some of them secretin was administered daily by subcutaneous injection. By the end of the third week in the secretin treated rabbits, the erythrocyte count was back to normal and at the end of eight weeks was 27 per cent above the original level. In the untreated rabbits there was hardly any increase in the count for two weeks and it was scarcely back to the original level at the end of eight weeks. Also the secretin treated rabbits put on weight more rapidly than the others. There can hardly be any question that the secretin facilitated the recovery of these animals from a dietary anaemia.

Preparations of secretin have been made by various means but none of them appears to be absorbed from the gastro-intestinal tract in active form¹⁹. At least pancreatic secretion does not follow oral administration. It does not necessarily follow that the haematopoietic effect of the preparation cannot be obtained in this way.

One of our preparations of secretin has been administered subcutaneously to man. Some pain occurred but there was no other untoward effect. A definite increase in red corpuscle count was obtained. The white corpuscles were not counted.

Solutions of secretin preparations do not keep more than a few days at most, but a satisfactory dried powder can be obtained readily²⁰. This powder is very soluble and its solution can be sterilized by boiling. The powder will keep several months at least.

Summary

Diet is most important both in the production of anaemia and in blood regeneration. The dietary factors which have been found to favour production of haemoglobin and red blood

corpuseles arranged in the order of their importance are cooked beef liver, lean beef and beef heart, spinach and beet tops, fruits, and other green vegetables. Rigidly controlled experiments fail to show any beneficial effect upon blood regeneration of arsenic or germanium dioxide, and iron is effective only if the iron reserve of the organism is exhausted. Favourable results have been obtained by the oral administration of dried powdered spleen and red bone marrow in the majority of cases of secondary anaemia in which the combination has been tried. Experimental findings strongly suggest a trial of secretin in similar cases.

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LEPROSY IN MONTREAL

REPORT OF A CASE*

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THE interest in this contribution lies chiefly in the fact that leprosy is rare in Montreal. With the exception of another patient, admitted to the Royal Victoria Hospital in 1925, in the final stages—one has to go back to 1900, to the days of Wyatt Johnson, for an authentic hospital case.

The patient, a Chinese laundryman, aged thirty-five was admitted to the Montreal General Hospital, August 27, 1925, complaining of skin eruption and general weakness.

Previous History.—He had lived in China until 1913 when he came to Canada. He was employed as a ship-builder in China, and worked in a Montreal laundry from 1917 to 1921, when he returned to his native land. Eighteen months later he again emigrated to Canada. There is

no history of skin disease in his family, nor contact with a similar affection. In 1918 he had gonorrhœa for three weeks but there is no history of syphilis. In 1923 there were pains in several joints—without fever—lasting a fortnight, and insufficient to confine him to bed. He was fairly healthy until the present illness, though he states that he voided about ten times a day and three times at night for several years. Pain seems to have been absent.

In April 1925, five months ago, subcutaneous nodules appeared over the left malar bone. Within the next few weeks others developed rapidly on the face, forearms, hands and legs. The largest nodule, on the left leg, attained the size of an almond within a month. None of the nodules have disappeared. He has not been able to work for ten weeks. There is nocturnal pruritus and transient, dull pain in the feet,

* From the Dermatological Department under Prof. G. Gordon Campbell, Montreal General Hospital.

but not elsewhere. He is quite chilly at times and there is gradually increasing weakness and general malaise. There is no headache. The appetite is fair, with marked thirst and constipation; nausea and vomiting he suffers from rarely. Sweating is diminished. Shortly before coming under our observation two salvarsan injections were given, intravenously, and the patient states that the nodules immediately enlarged. In confidence, the patient stated that his chief reason for seeking admission was to obtain food, as his compatriots suspected leprosy and refused to prepare his food, or to care for him.

The larger nodules include the skin, but many are subcutaneous, and surmounted by intact skin. The nodules are most prominent on the face, especially about the eyebrows, on the forehead and malar prominences, occurring with marked symmetry, and resulting in a leonine appearance. Lesser nodules are found on the remainder of the face and on the neck. Nodules constitute more than half of the ears. The chest and front of abdomen are clear, except for a few macules on the left costal margin. The nasal and oral mucous membranes are devoid of lesions and the scalp is unaffected. The outer halves of the eyebrows have almost disappeared.

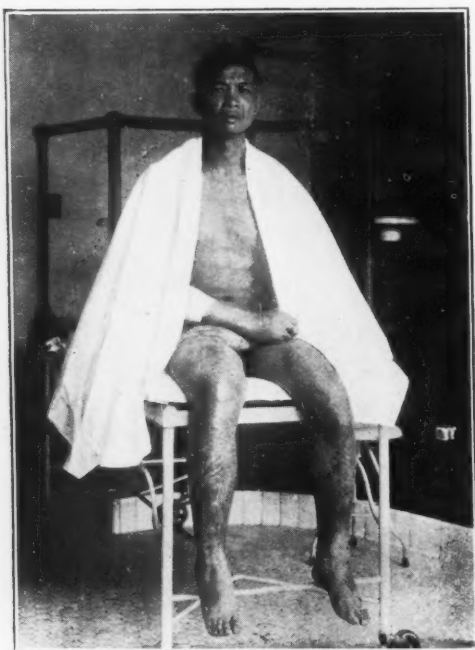


FIG. 1.—Leprosy five months after onset with typical Ichthyosis-like condition of the legs.

The *family history* is irrelevant. Father, mother, three brothers, three sisters, wife and one child are all well in China.

Condition on admission.—A well nourished Chinaman, who walked into hospital looking ill, assuming any position, breathing easily.

Integumentary system.—The main feature of the eruption consists of nodules varying in size from a split pea to an almond, grey, brown or pink. These are firm and rounded, raised, according to size, up to a quarter of an inch. There are no blebs or ulcers, nor is there any

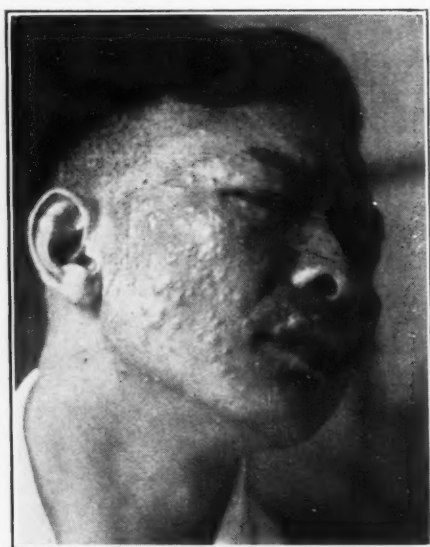


FIG. 2.—Leprosy, nodular, five months after onset.

The upper arms contain very few nodules, but the forearms are studded with them, especially along the course of the ulnar nerves. Nodules from the forearms were excised for biopsy. On the palms are several small nodules, the largest the size of a pea. The backs of all phalanges are affected. The finger nails are intact. The proximal phalanx of the right mid-finger is swollen and red. Aspiration yielded very little serum. On the lumbar region and slightly to the right of the centre there is a plaque of thickened, dusky red, integument—roughly ovoid, with definite, but irregular margins, slightly raised, surmounted by large scales. This area measures about seven inches either way

and the colour is deeper at the periphery. The central half has faded until the skin is practically normal.

The right leg, from the upper thigh to the ankle, is ichthyotic. The skin is thickened, inelastic and dusky red, with accentuation of the creases, and with fine and coarse scaling. As a result, the right leg has the appearance of elephantiasis. The remainder of the legs, feet and soles is almost as nodular as the forearms, but there are two irregular clear islands in the area over the right knee. There is a very large nodule over the upper extremity of the left fibula. The plantar nodules, like the palmar, are surmounted by marked erythema. The toe nails are dry, thickened, cracked and partially deficient.

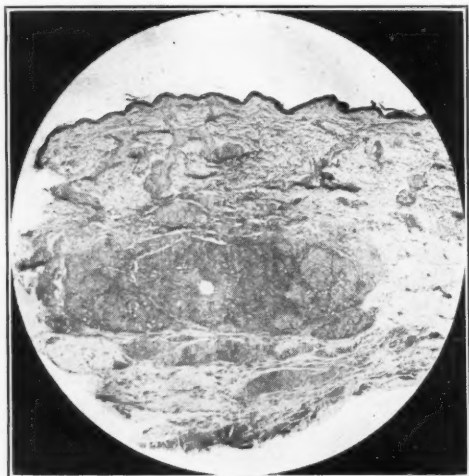


FIG. 3.—Section through a leprosy nodule, from the forearm, under low power. The detail structure of the nodule is that which is seen in a typical leprosy nodule. The dark-staining central area represents the lesion which is subcutaneous.

Examination of the nasal and oral cavities and eyes, reveals nothing abnormal. The lungs are clear throughout. The heart is not enlarged. There is a sustained systolic murmur, which is not transmitted. The first sound at the base is obscured by a rough sustained murmur; best heard over the pulmonary cartilage. A faint diastolic murmur is heard over the third rib in the midline.

The glands show little if any change, except for firmness of the epitrochlears and some enlargement of the cervicals.

Examination of the abdomen is negative.

The abdomen is soft, with no mass, spasm or tenderness. The liver is not palpable and the spleen is soft and barely felt.

The genitalia—There is a small white fibrous sear on the dorsum of the penis near the prepuce and a soft oedematous swelling near the frenum. Otherwise, the genitalia are normal. The reflexes are, apparently, normal. The right knee jerk is slow but this may be attributed to the enlargement described. No anaesthesia is found, except what might be expected in similar papules from any cause. The bones and joints are normal. X-ray of the hands and tibiae show clear-cut, bony outlines. The Wassermann is negative. The sugar tolerance test shows evidence of delayed assimilation and a few pus cells.

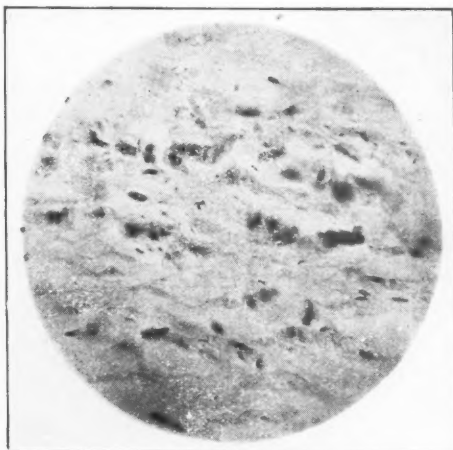
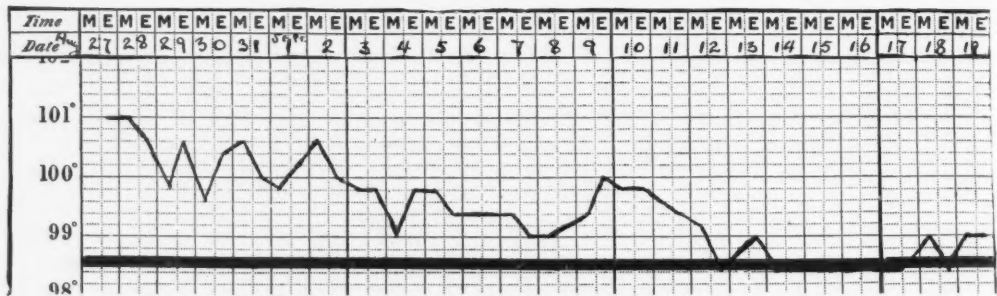


FIG. 4.—Microphotograph from a section of a leprosy nodule with leprosy bacilli, single and in clusters, intra- and extra-cellular.

The urinalysis:—Spec. grav. 1018, acid, slight trace albumen, no sugar. Microscopic—25-30 pus cells to high power field.

Clinical course to September 20th.—The temperature range was 90° to 101° for the first two weeks and then remained normal for a week followed by a gradual rise. The pulse was 96 to 120. The appetite was very fair and the bowels active, but there was a gradual increase of weakness, nocturnal pruritus and chilliness; his meals were taken in the sitting posture. As the admission was for the diagnosis only, no specific treatment was given.

After remaining in hospital three and a



Typical chart of leprosy, showing alternating pyrexial and apyrexial periods. Subsequent rise of temperature was reported after patient reached Tracadie, N. B.

half weeks, the patient was removed to the Lazaretto at Tracadie, N. B.

Summary

(a) Insidious onset and course. (b) Nodular out-growths and facies leontina. (c) Areas of pigmentation. (d) Falling of eyebrows. (e) Disturbances of sensation and trophic changes. (f) Ichthyosis-like condition of the legs. (g) Moderate temperature for two weeks followed by an afebrile period. (h) Negative Wassermann. (i) Delayed assimilation of sugar. (j) Biopsy positive for *Bacillus lepra*.

Pathological report by Dr. L. J. Rhea.—Section from a nodule on the arm shows acid-fast bacilli, but not in large numbers. These are comparatively easily decolorized and coarse granules are easily demonstrable. So-called "foamy cells" are shown in the sections, but fewer than usual. Some of the cells contain twelve or more bacilli.

Discussion.—That the disease was contracted in China before 1922 may be assumed. Walker¹ cites a case where a Russian Jewess aged seventy had lived in Scotland over forty years and developed the disease under his observation. The diagnosis of leprosy is easy in typical cases but at other times is very difficult. Fordyce and Wise² refer to an American leper whose lesions appeared fifteen years before the diagnosis was made, as small discoloured areas on the left leg, without disturbance of health. As in our case, leprosy has frequently had anti-syphilitic treatment. Through the ages lazarettoes have not been free from syphilis, psoriasis, tuberculosis, furunculosis, lupus erythematosus and alopecia areata. Moses' description in Leviticus indicates that the term "leprosy" covered a wide range of diseases. The waxing and waning of temperature is frequently seen, registering about 101° for a week or so, followed by a period of normal temperature. A sugar tolerance test showing

delayed assimilation is of interest, as the literature on this subject is scant.

Since January, 1916, Canada has treated thirty-nine lepers at Tracadie, N. B., and Bentinck Island, B. C. The number of patients at Tracadie, N. B., has decreased since 1851 from thirty-seven to twenty-four. One-half of those treated were native Canadians, one-third were Chinese and the balance were Assyrian, Chilean, Kanaka, Irish, Japanese, Doukabor, Iclander and Russian Jew.

There have been fourteen deaths during the decade and nine are declared "non-infectious, disease checked" though six of those remain at Tracadie, having no other home, and are too mutilated to work. The Iclander has been at Tracadie since 1897.

Leprosy is considered the least transmissible of any contagious disease.

The Immigration Act provides for the return of a foreigner found suffering from leprosy within five years of his arrival in Canada. After five years he becomes our burden until death or cure. A federal act of 1906 provides for the compulsory segregation of lepers, upon the request of local authorities.

To Professor G. Gordon Campbell, Chief of the Department of Dermatology and Professor J. Rhea, Director of Pathology, my thanks are due for their clinical and pathological assistance and stimulation.

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PLASTER SHELLS IN THE TREATMENT OF TUBERCULOSIS AND FRACTURE OF THE SPINE

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PLASTER shells have been designed to splint the spine whenever splinting is necessary on account of disease or injury. They have been in use for several years in the Massachusetts General Hospital and in the Children's Hospital, Boston, and were brought to our attention through the writings of Lloyd T. Brown and R. P. Swartz of that city. Since adopting them some two years ago, they have proved so satisfactory that the writer has been prompted to bring them to the notice of this Society. We have found them particularly useful in the after treatment of fusion operations upon the spine, and also in the management of recent fractures, and of those cases of spinal tuberculosis which for one reason or another are not operated upon.

The shells are made to fit accurately, one the posterior, and the other the anterior surface of the body. The patient lies the greater part of his time on the posterior shell. Whenever he is to be turned, the anterior shell or lid is placed over him and the two shells are fastened together by tying strips of heavy calico bandage around them. The patient is then turned, the posterior shell taken off, and he lies upon the anterior shell until it is time to turn him back again. During the process of turning there is no torsion of the spine and no movement at the seat of the lesion, and consequently no pain. Both shells extend from just below the neck to the middle of the calf in all cases. If the lesion is above the fifth or sixth thoracic vertebra the posterior shell is continued upward to support the occiput, and if it is desired to splint the cervical spine the anterior shell should include a chin support.

The posterior shell is made first, and this

should be done a day or more before it is to be used. The patient is placed on a table lying face downward supported by pillows and sandbags. Much depends upon one's success in placing the patient in the best position. In tuberculous cases as much correction of deformity as possible without causing pain should be obtained. The chest must be supported so as to allow for full expansion of the lungs. The head and neck should be in a comfortably extended position, the thighs not over-extended and somewhat abducted, and the knees slightly flexed.

When the position of the patient is satisfactory a sheet of thick felt is put over him and cut out so as to cover the posterior half of the body and limbs. Extra felt pads are sewed to this over the more prominent bony projections, and gores are cut wherever necessary to secure an accurate fit. The felt is then bandaged to the trunk and limbs and the patient is ready for the application of the plaster bandages. These are put on in strips longitudinally and crosswise. Slow setting plaster is used, and it is necessary for two to work applying the bandages, one standing at each side, so that there will be a thick layer of plaster before the deeper layers begin to set. This permits of careful moulding in two situations especially: along the erector spinæ muscles, thus permitting them, and not the spinous processes, to take the weight of the patient; and in the loin, so as to keep the lower ribs pressed forward and allow for full expansion of the lungs. Reinforcing irons are used, along each side of the body part, bridging over the junction of the body and thigh parts, and at the knees, as well as across the distal and proximal ends of the body portion. These are bent to fit the frame accurately after it has been moulded, and put

* Read before the Winnipeg Medical Society, April 17, 1925.

on before the superficial layers are set, and then covered with fresh plaster. It has been found advisable also to bridge across the space between the two knees with plaster reinforced with iron, and if the head is included in the frame an iron is used at each side of the neck.

When completed the shell is lifted off and set aside to dry. Usually the felt will be sufficiently adherent to the plaster. If it is loose in places it can be cemented down by using a little plaster cream. The next day or as soon thereafter as convenient the patient is placed in the posterior shell and the anterior shell made similarly and set aside to dry.

The indications in the mechanical treatment of Pott's disease are first to provide rest for the diseased bodies, and rest here means not only freedom from movement but freedom from weight bearing; and second to prevent deformity from increasing, or if possible without interfering with the process of repair to diminish any deformity that may be present by developing compensatory curves above and below the lesion. These indications can be met by a prolonged period of recumbency in a suitable position. The double Thomas's frame and the Bradford frame were devised with this end in view, and both have given excellent results. Neither, however, fits the back as accurately or gives as much freedom in turning the patient as could be desired. A double plaster jacket spica gives excellent fixation and permits of turning, but to a certain degree it constricts the vital organs, interferes with the nursing care, and with heliotherapy. The use of internal splinting by means of bone grafts as devised by Hibbs and Albee, producing a bony union of the posterior parts of the diseased vertebrae and of those immediately above and below gives adequate fixation, and therefore perfect rest, and is to be recommended whenever it is possible. These are, however, formidable operations, and there is a percentage of patients with Pott's disease that cannot safely undergo them. This is especially true of those with active pulmonary lesions. Such individuals have in a long period of recumbency their only hope of cure. One point in their favour is that while they are "taking the cure" for the lung condition they can be getting good treatment for the spinal lesion. In them the plaster shells fulfill all indications,

securing rest and relief of pain, with prevention of deformity, and heliotherapy possible. As the spinal lesion improves, the patients can spend more and more time lying on the anterior shell, and gradually begin to raise the body up from it, thus developing the erector spinae muscles, as recommended by Rollier.

We have come to use the shells as a routine in the post-operative management of those patients on whom a fusion operation has been done for Pott's disease. In our clinic, fixation by means of multiple grafts as introduced by Hibbs, is the operation of choice. Immediately following this operation the operative area of the spine is very lax indeed, and if not carefully protected will tend to sag into the position most favoured by gravity. This is so because of the nature of the operation: it is necessary to clear the spinous processes and laminae of all muscle and ligamentous tissue as far out as the lateral articulations, for at least six segments, more often for more. As a result, if care is not taken to prevent it, it may be found after the spine has become solid, that the deformity has actually increased; whereas with the use of the shells it can frequently be diminished. Other striking results of the use of the shells are that the patient is more comfortable and the nursing is made easier, important considerations following operations of this magnitude.

During the manufacture of the posterior shell no allowance is made, as a rule, for the copious post-operative dressings, so that when these are applied they act as a pad to press the diseased area gently forward. Throughout the succeeding weeks this pad can be increased, if thought desirable.

It is a great comfort to the patient and to those in attendance upon him to know that he can be turned over any time after the first few hours. We have found it desirable to have him turned at least once a day from the beginning. While he is lying on the anterior shell, the back is attended to, and any reddened area is treated and protected from further pressure. During the third month in bed, if free from pain and muscle spasm, he is encouraged to raise the thorax while lying face downward, thus tending to diminish the deformity by developing compensatory curves above and below the lesion. After the first few weeks sun or

lamp treatment can be given without any inconvenience from the operation.

Sepsis of the wound is a possible accident following these operations. This occurred in one of our cases, number 15752 P. R., age twenty-three. He was a tall man rather heavily built. Although the only x-ray finding was a narrowing of the space between the bodies of the last thoracic and first lumbar vertebrae, he had had a sinus in the lumbar region for over a year, which however had been closed for a few weeks. The usual elaborate precautions to prevent infection were taken, but on the fourth day when the wound was examined because of a rise of temperature it was found to contain large quantities of reddish pus. Apparently the old abscess had worked through



FIG. 1.—Shows patient with Pott's disease of the lumbar spine, lying on posterior shell.



FIG. 2.—Same patient as Fig. 1, with anterior shell tied on, being turned over.

into the deeper parts of the wound. Subsequently it broke open for the whole of its length, about ten inches. Under moist dressings changed every few hours at first, healing progressed rapidly and was complete in eight weeks. Anyone who has had a similar experience will realize what an advantage it was to be able to turn the patient as often as desirable, without causing torsion or sagging of the spine.

In the management of patients with fracture of the spine, the shells have been equally satisfactory. Needless to say, when there is a complete cord lesion not much is to be expected. However the extent of the cord lesion cannot always be accurately diagnosed at the beginning, and even in apparently hopeless cases the degree of recovery with this method of treatment may be very gratifying. Moreover, cases of a crushing fracture of a body of a vertebra in which the cord has in great measure escaped permanent injury are not uncommon, and under these circumstances the plaster shells have proved invaluable. The following is a striking case.



FIG. 3.—Same patient as in Figs. 1 and 2. The doctor is lifting off the posterior shell, leaving the patient lying on the anterior shell.

Case number 15155 G. H. J., age twenty-four, came under observation on August 31, 1923—about twenty-four hours after his accident. He was working in the sitting position painting a grain elevator, suspended forty feet above the ground, when the tackle gave way. He alighted on the buttocks, and the tackle hit him on the head. When he regained consciousness eight hours later, he complained of severe pain in the lumbar region. He was brought to Winnipeg by train, a distance of one hundred miles.

When examined he was lying on his back with his knees drawn up. Any attempt to move him caused severe pain in the lumbar region. He suffered discomfort from a distended bladder, although he had urinated once since the accident. No paralysis or anaesthesia was detected. However, the saddle area was not examined. The normal lumbar lordosis was replaced by a fullness which felt indurated and was extremely tender. The x-ray (Fig. IV.) showed a crushing of the anterior part of the body of the first lumbar vertebra, as well as fractures of both transverse processes of the last thor-

acic and upper two lumbar vertebrae and of the right transverse process of the third. The lumbar lordosis was replaced by a curve, convexity backward.



FIG. 4.—Case of crushing fracture of first lumbar vertebra described in the text. Condition before treatment was begun.

Next morning he was anaesthetised, and manipulation carried out by Dr. Galloway. Patient was turned on his face, sandbags were placed under the pelvis and under the upper part of the thorax, so as to allow the lumbar region to sag forward. Strong traction was then made on the head and shoulders and on each foot, while the operator pressed firmly on the lumbar spine. This resulted in a marked improvement in the contour of the region, the lumbar lordosis being restored. The posterior shell was then made, traction being maintained meanwhile. As soon as this was hardened he was turned over, so as to lie upon it, and the anterior shell was made.

When he recovered from the anaesthetic the

acute pain was gone. He was turned over every day and allowed to lie as long as he wished on the anterior shell. Beginning the second day regular catheterization was instituted. Retention was complete at first, but in three weeks he had regained normal bladder control.



FIG. 5.—Same spine as in Fig. 4 after three months' treatment.

Eight weeks after the manipulation a Hibbs' operation was done, fusing the last thoracic and all the lumbar vertebrae. He continued to lie on the frames for eight weeks after operation, when a plaster jacket was applied. (Dec. 13th.) An x-ray picture taken about that time shows a gratifying degree of improvement. (Fig. V.) He wore the jacket for eight weeks. He was last seen in September 1924, just over a year after his accident. Although he complained of a burning sensation in the right buttock and had a saddle area of anaesthesia with loss of cremasteric and anal reflexes, and of the right Achilles jerk, he had no paralysis and no pain, and was back at work.

Unusual Bile Duct Visualization by Roentgenograms of Barium Meal.—Edwin Habbe, Boston and Lester A. Smith, Indianapolis, report a case in which the intrahepatic bile ducts were filled by the barium meal, evidently through a spontaneous cholecystoduodenostomy, and were clearly visualized. It is suggested that the bile ducts are probably filled in a similar manner by duodenal contents, after

meals, particularly when the patient lies down after eating. The retention of the barium in the ducts indicates that food material, with its accompanying bacterial content, must be present in the bile ducts at all times. Although this marked abnormality has been present probably for five years, it has caused no functional change, so far as can be determined by the usual liver function tests.—*Jour. Am. Med. Ass.*, Feb. 13, 1926.

A CASE OF CORROSIVE SUBLIMATE POISONING BY THE GENITAL TRACT

BY JAMES MILLER

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HISTORY of the case. On July 31st a girl of about eighteen years of age was taken suddenly ill in a house in Kingston where she had just gained admission. The nearest doctor was summoned and on his arrival he found the girl lying in a pool of blood. On examination a four-months fetus was found born all but the head. Subsequent investigation revealed the following history. On the evening previous to the occurrence a douche of fluid afterwards ascertained to contain corrosive sublimate was given by means of a rubber syringe with a view to procure abortion. An unconfirmed report stated that some time previous to this a wooden implement had been thrust by a different person into the genital tract with the same object in view. It is perhaps needless to say that neither of these operators were medical men. The corrosive sublimate used was in the form of tabloids and the statement was made that one of these was added to about a pint of water which, it was estimated, would give dilution of approximately one in a thousand parts. The physician first called in, attempted by abdominal pressure to procure the birth of the placenta but owing to the intense abdominal pain complained of he desisted. The patient was accordingly despatched to Kingston General Hospital where a thorough investigation was made. At this time the temperature was normal, the pulse 122 and the respirations 44. On examining the genital tract blood was found flowing as after a normal labour. The vaginal mucosa was of a dark greenish-black colour presenting the appearance of necrosis. On the following day a curettage of the uterine cavity was done and placental tissues removed. It was noted by the operator that in his manipulations the vaginal mucosa was friable and several tears resulted. A slight tear of the perineum also occurred and was sutured. The patient complained of persistent abdominal as well as pelvic pain. She vomited and hiccuped

at frequent intervals. She was unable to pass water and was therefore catheterized but without result. Throughout her stay in hospital which lasted six days she had complete suppression of urine. Owing to the vomiting the patient was unable to take nourishment. The respirations and pulse became shallower and more irregular. On the fourth day the patient vomited a considerable quantity of blood and the bleeding from nose and mouth as well as from stomach continued until her death. She became gradually more and more drowsy but at intervals was restless and often wandering. A blood urea test was done on a sample of blood taken some hours before death. The result obtained was 120 mgm. of urea per 100 c.c. of blood. She died as stated on the seventh day after her admission to hospital.

Post mortem report.—The autopsy was performed about two hours after death. The body was that of a well developed and well nourished young woman. There was a slight posterior tear in the perineum closed by three sutures. There was no excess of fluid in any of the serous sacs. On examining the peritoneal cavity a loop of bowel was found adherent to the fundus uteri. At this point the muscle of the uterus appeared necrosed and there was fibrinous exudate on the surface. The adhesion between the bowel and the uterus was readily broken down. The heart was enlarged due mainly to a dilatation of the right side. No clot nor thrombus was present. The valves were normal with the exception of the mitral which showed a small area of thickening towards the margin of the septal cusp. The aperture admitted two fingers easily. The wall of the left ventricle was somewhat thickened and the muscle was pale. The heart weighed 262 grammes. The aorta was normal. The right lung weighed 242 grammes and the left 192. Both showed relative absence of pigment. There was slight puckering at both apices and two calcareous glands were found at the roots. No consolidation was present in any part of either lung. The œsophagus was normal. The stomach contained a considerable amount of bile-stained material with dark brown shreds in it. The mucous membrane appeared pale and there were no visible hæmorrhages. The coils of intestine showed some reddish staining of their peritoneal aspect. On opening them they were found to contain some dark semi-fluid material. On washing this away the mucous membrane showed no abnormality. The pelvic colon contained some dark coloured blood-stained faeces. The mesenteric and retro-peritoneal glands were somewhat enlarged, but there was no evidence of caseation. The appendix was elongated but normal. The liver weighed 1825 grammes. It was pale and soft. The gall

bladder was distended with bile. The spleen weighed 140 grammes. On section it was light red in colour and moderately firm. The Malpighian bodies were not prominent. The pancreas showed nothing of note. Both kidneys were somewhat swollen. The right weighed 167 grammes and the left 195. On section there was marked pallor of the cortex which was swollen and somewhat friable. The capsule stripped easily leaving a perfectly smooth and abnormally pale surface. No urine was found in the bladder and there was no lesion of the mucous membrane. The vagina was dark grey, almost black in colour owing to superficial necrosis. There were several longitudinal tears in the mucous membrane revealing the submucous tissue which was reddened from hæmorrhage. The uterus was enlarged measuring three and one-half inches from fundus to cervix. Several hæmorrhagic spots were visible on the peritoneal aspect, also an area of fibrinous exudate on the left side of the fundus under which the muscle was pale from necrosis. On section the necrotic area extended as far as the inner surface but a probe showed no channel of communication between the interior and the peritoneal coat. The mucous membrane of the uterus was rough and irregular from adherent blood clot.

The brain weighed 1525 grammes. It showed no abnormality on the surface. On section, beyond the evidences of edema there was no change.

Microscopic findings.—The most important changes were found in the urogenital tract.

The kidneys showed as is usual in such cases profound alterations. These were met with chiefly in the convoluted tubules which were uniformly filled with debris of a granular nature staining more or less deeply with eosin. In part this debris was formed of disintegrated epithelial cells derived from the lining of the tubules. Such cells could be seen lying partially destroyed in the necrotic content of the tubules. In addition to these polymorphonuclear leucocytes were

present in considerable numbers and here and there large masses of red blood corpuscles. Although literally many scores of sections were examined (the preparations being issued to over a hundred students for teaching purposes) no evidence of calcification was found in any of the necrotic plugs. This fact is commented upon below. A further point of interest as regards the tubules was the presence in most of the tubules of a layer of remarkably healthy epithelium underneath the necrotic cast. These cells still attached to their basement membrane stained well and possessed in many instances more than one nucleus. Here and there mitotic figures were found. These appearances may be taken as evidence of regeneration on the part of the tubular epithelium. Many of the cells both those attached and those thrown off were distended with granular material staining an intense pink with eosin. Some of this material assumed disk-like shapes suggesting red blood corpuscles. The appearances of necrosis were not so well marked in the collecting tubules but they also were filled with cellular debris and granular material. The glomeruli for the most part appeared swollen, filling up the space. Occasionally where a gap was visible between the tuft and Bowman's capsule swelling and desquamation of the lining cells could be seen. No hæmorrhages into the space were seen and no thrombosis in the capillaries of the tuft. The endothelial cells of the capillaries were swollen and the whole structure of the glomerulus appeared more cellular than usual. No change of any importance could be seen in the stroma or in the vessels of the kidney. The bladder showed an interesting condition. No urine had been passed by the patient for seven days but no doubt a small quantity of a highly concentrated fluid had trickled into the bladder. As evidence of this there was a quite distinct catarrhal cystitis as indicated by desquamation of epithelium and infiltration of the submucous coat with cells chiefly of a mononuclear

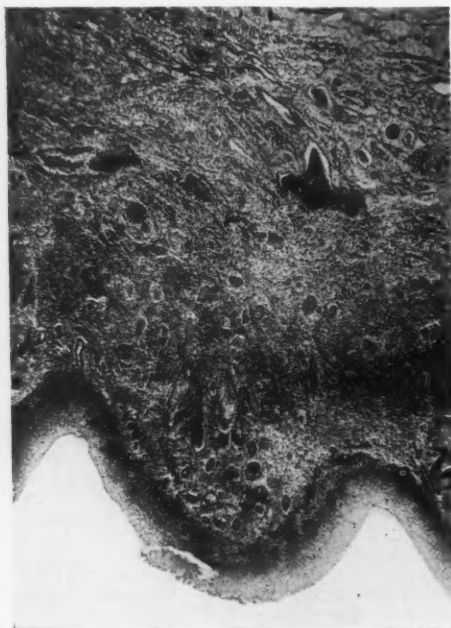


FIG. 1.—Shows low power view of vaginal mucosa with superficial necrosis, congestion, thrombosis, hæmorrhage and leucocyte infiltration.



FIG. 2.—High power view of kidney showing swelling and shedding of epithelial cells. One tubule in centre blocked with necrotic cells and debris.

type. The *vagina* showed coagulation necrosis of the surface epithelium, the cells having lost their individuality and the nuclei being unstained. There was a general infiltration of this necrotic layer with polymorphonuclear leucocytes especially towards the deeper parts and here and there masses of bacteria could be seen. In the sub-epithelial tissue there was an intense congestion of vessels, widespread hemorrhages and areas of cell infiltration. Many of the vessels were the seat of thrombus formation. A piece of the *uterus* taken at the junction of the necrotic area with the normal tissue showed loss of staining in the dead portions, cell infiltration with polymorphonuclear leucocytes and masses of cocci and bacilli in the necrosed parts. Extensive areas of hemorrhage were seen in the necrosed parts and many of the larger blood channels were thrombosed. The *stomach* showed numerous small hemorrhages into its mucosa. There was also a fairly well marked infiltration with polymorphs and eosinophiles. The *small intestine* showed similar but less marked changes. The *liver*, *heart muscle* and *pancreas* showed evidence of pronounced toxic change. The *spleen* was intensely congested and one small fibrous nodule suggestive of old healed tubercle was found. The *thyroid gland* showed abnormal distension of its acini and some catarrh.

Summarising the microscopic appearances it may be said that these confirmed the gross morbid anatomical findings. The kidney presented the usual appearances in the case of corrosive poisoning viz. necrosis of the lining cells of the tubules, although calcification of the necrotic casts was absent. There was evidence of a widespread damage to vessels in the hemorrhages into the mucous membrane of the stomach. These hemorrhages were not visible to the naked eye. The cystitis due to the irritation of a concentrated urine is an interesting observation in the case. The microscope revealed large masses of germs in the necrosed vaginal mucosa and in the wall of the uterus, showing that septic absorption must have played some part in the fatal issue.

The pathological investigation revealed quiescent tuberculosis of lungs and bronchial lymph glands also a slight chronic endocarditis of the mitral valve. Neither of these lesions had any bearing upon the fatal issue. The main conditions were (1) a localised laceration of the uterine wall with a plastic peritonitis overlying this; (2) necrosis of the vaginal mucous membrane due to the use of a chemical poison; (3) acute catarrhal nephritis (4) Toxic changes in the parenchymatous organs. Death was undoubtedly caused by the suppression of urine resulting from the nephritis which led to uræmic poisoning, but septic absorption from the vaginal and uterine cavities played a part.

Comments on the case from a pathological point of view. Poisoning from corrosive sublimate is not an uncommon occurrence. The avenue of entrance into the body is usually the alimentary tract, the poison being ingested either accidentally, with intent to commit suicide or administered with murderous intent. Poisoning by the genital tract is far less common, but is certainly more frequent than is generally supposed. This matter will be dealt with in discussing the clinical aspect of the case.

The mode of action of the poison, however it be ingested, is always manifested on the urinary secretion. As a rule there is a more or less

complete suppression of urine. As to the mechanism by which this is brought about there are at least two distinct views. There is first the older view, generally accepted since the time of Virchow, that corrosive sublimate has a specific action upon the lining epithelium of the urinary tubules, causing a necrosis followed in the second week after the poisoning by a deposition of calcium salts (Askanazy, Aschoff's *Pathological Anatomy*, 1921, Bd I. p 131), and that the suppression is due to a blocking of the tubules with the epithelial debris. The calcification is one of the stock examples of calcareous deposit following necrosis cited in the text books. So far as this case throws light upon the question it may be said to bear out Askanazy's statement that calcification does not occur unless the patient lives for more than one week after the administration of the poison there being no evidence of this condition although some scores of sections from different parts of the kidneys were examined. The other view of the mode of action of the poison, partly derived from a study of the condition experimentally produced in animals, is that action is primarily upon the circulation and the vessels of the body generally and only secondarily upon the kidney tubules. A recent experimental piece of work is published by Strake (*Inaug. Diss. Breslau* 1920 ref. Cbl. f. Path. Bd. 31. 1920). This observer saw in rabbit's kidneys exposed and examined in the living condition under the binocular microscope fifteen minutes after the administration of a dose of the poison, first a distension of the vessels and a slowing of the blood current until stasis occurred. In the course of the slowing of the circulation red cells passed out from the glomerular capillaries into the tubules. There the corpuscles break down, and the products of their disintegration act upon and damage the lining cells of the tubules. This view is supported by certain pathologists from the human standpoint as for example Soli (*Archivio di Antropologia Criminale*. Vol. xlv. p. 396. 1924) who stresses the glomerular changes observed in a human case of poisoning by way of the vagina. This observer also notes the red globules within the epithelial cells seen in our case, but does not suggest an explanation for them. In the case under review as stated above glomerular changes were not striking.

A further interesting point in our case is the extent of the regenerative changes on the part of the epithelium lining the tubules. These changes are particularly striking and well seen probably on account of the fixation of the tissue some two hours after death. MacCallum in his text book (1924, p. 283) draws attention to this regenerative change in such cases.

Comments upon the case from a clinical point of view. In an exhaustive paper upon the subject the Italian writer Soli (loc. cit) states that corrosive sublimate has been administered or taken by the genital tract for the following purposes (1) as a contraceptive (2) with a view to procuring abortion (3) as an antiseptic douche (4) with murderous intent. The drug has been given in the form of a douche and as tablets undissolved. In the case cited by him one pill was introduced into the vagina with fatal result. He stresses the fact that even the intact vagina and still more the uterus after parturition absorbs the poison with avidity. Fatal results have been recorded when the dilution of the poison was as high as one in four thousand, more commonly the dilution in fatal cases has been one in a thousand or less. The puerperal cases are of course the most dangerous, but even the normal vagina is capable of rapid absorption. Soli claims that it is questionable whether concentrations of one in two thousand even under normal conditions of the genital mucosa are exempt from danger. He concludes "Such frightful results from the use of sublimate solutions for endo-uterine and vaginal irrigation justify its complete exclusion from obstetrical and gynaecological practice."

Comments on the case from the medico-legal point of view. From the medico-legal point of view the following may be said. There could be no doubt at all from the admission of the in-

dividual who administered the douche and from the clinical and pathological findings as well as from the statement of the woman, that death was due to poisoning through the mercurial vaginal douche. There was, however, also damage to the uterine substance which could not have been produced by a douching with a rubber tube. This bore out a statement by the defence that an attempt was made by another person to procure abortion by the passage of a rough instrument (a wooden ruler). In answer to this it might be advanced that such damage might be due to the curettage at the hands of the surgeon. This would of course be highly improbable, but the point is of minor importance as it does not alter the main fact of the case that the corrosive sublimate douche caused the death of the patient. The laceration of the uterine musculature as it occurred before the douching, would increase the absorptive surface, but this was large enough in any case. There is this to be said, however, that the abdominal pain and tenderness complained of by the patient was probably due to the laceration of the womb and the consequent localized peritonitis, proved to exist at the autopsy.

A word might be said as to prognosis and treatment. These cases appear to go through a definite course and in spite of douching and drugs, however early this treatment be applied, the fatal issue is to be looked for within two weeks. This undeviating course is no doubt due to the fact that an albumin compound is formed between the mercury and the tissues and fluids with which it comes in contact. This compound is soluble in excess of albumin. Thus a rapid entrance into the blood is obtained. Favourable results have been reported with sodium thiosulphate administered intravenously (J.A.M.A. Dec. 27, 1924). In other instances this treatment has failed.

Use of Castor Oil in Treatment of Bacillary Dysentery.—Boase sets forth the greater value of castor oil, administered in repeated small doses, over magnesium sulphate in the treatment of bacillary dysentery. In the epidemic reviewed by Boase all dysenteric patients were

allowed full diet consisting of cooked bananas or sweet potatoes, tea, soup, with meat when available, sugar cane, and milk when the supply would meet the demand. No ill effects were noticed from this innovation.—*Kenya Med. Jour.*, Nairobi, E. Africa.

A CASE OF ENDOTHELIOMA WITH XANTHOCHROMIA*

BY L. M. LINDSAY, M.D.

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R. L. was a boy, aged three years, when admitted to the Children's Memorial Hospital on February 17, 1925. His complaints were: Headache, vomiting, convulsions. He had been a healthy boy until November, 1924, (three months prior to admission), when he began to vomit. This vomiting occurred usually in the morning and bore no relation to the taking of food. At first it recurred every two or three days, and then became a daily occurrence. At this time no change was noticed in his disposition. He played about as usual, before and after the vomiting. His appetite was good and his bowels regular. He had measles in December. This had no apparent effect on the vomiting, which continued as usual.

On January 29, 1925, the boy had his first convulsion. This was general and lasted about twenty minutes, leaving him prostrated for some hours. He then began to have headaches, sometimes frontal, sometimes vertical. Since then he has remained in bed. The vomiting has continued unabated and he has had two more convulsive seizures. No paralysis was ever noted, and no oedema of body or puffiness of face, although nephritis had been diagnosed on account of the albumin and casts which were present in the urine. He was sent to the hospital because of the headache, vomiting and convulsions, which with the urinary findings suggested uremia to the physician. There was nothing in the family history or in the boy's past history which seemed to have any bearing on the present trouble.

Examination on admission.—T. 99 2/5°. P. 110. R. 22. He was fairly well nourished and developed, but was pale. There was no puffiness or oedema. He seemed comfortable lying in bed. There was no general glandular enlargement, but the tonsillar nodes were large and his tonsils hypertrophied. Nothing abnormal was made out in the heart or lungs. The abdomen was also negative. The spleen was not felt and the liver not enlarged. His extremities appeared normal.

The nervous system.—His mind was clear, but he was irritable and fretful. No paralysis or spasticity was noted in any part of the body, nor were there any pathological reflexes. The pupils were equal and active. Examination of the fundi showed definite *optic neuritis*, the discs being congested and blurred. There was no ptosis, strabismus or nystagmus. Sensation was normal.

The urine was turbid yellow, 1026, acid, and contained a trace of albumen and a few granular and hyaline casts, but no sugar, acetone, blood or pus; there was a normal secretion of urine.

The blood count.—Red blood cells, 4,600,000; white blood cells, 10,200; hæmoglobin, 70 per cent. So far the only positive findings were the optic neuritis and a mild grade of nephritis. In order to account for the former, the following tests were made during the next few days: Pirquet test, negative. Wassermann, negative (both blood and spinal fluid). Blood urea, 16 mgs. Blood pressure, 90/60.

Lumbar puncture revealed the spinal fluid to be under moderate pressure. It was turbid and yellow and did not coagulate spontaneously. The cell count was 80, chiefly lymphocytes; globulin test was positive (Pandy); red blood cells and hæmoglobin were present; sugar and chlorides were in normal amounts; no tubercle bacilli were found.

In order to determine whether the xanthochromia was due to obstruction below the foramen magnum, a cisterna puncture was made. The fluid thus obtained was practically identical to that from the lumbar puncture.

The diagnosis was now an intracranial tumour. There were no localizing signs to indicate where this tumour might be.

Clinically the boy pursued a downward course. He continued to vomit and complain of headaches. He became drowsy and was very irritable when roused. He refused food and became emaciated. An acute otitis media developed during the first week of March. No further convulsions occurred; possibly owing to the frequent lumbar and cisternal punctures

* Presented before the third Annual Meeting of the Canadian Society for the Study of Diseases of Children at Ottawa, June 6, 1925.

that were made. Finally he became comatose, with more or less general rigidity.

He died on March 18, 1925.

Post Mortem Examination.—Showed nothing of any moment outside of the cranium.

The brain and meninges were somewhat congested and edematous. The convolutions of both right and left frontal lobes were flattened—especially the left. The dura appeared to be adherent to the anterior portion of the left frontal lobe, but on separating the parts a tumour mass about two and a half inches in diameter was seen abutting chiefly into the left frontal lobe, but also into the right. This tumour was not adherent to the brain at all but was found to be fixed to the dura. It was readily enucleated from the depression in the brain, in a ball and socket fashion. The tumour was quite firm but its surface was necrotic, and showed evidence of hæmorrhages.

Microscopic sections showed a very cellular tumour, the cells of which almost filled the picture. They varied in size and shape and did not conform to any specific type of tissue. There was a very little supporting stroma. Blood vessels were numerous and engorged; there was evidence here and there of hæmorrhages which displaced the tumour tissue. Thus it was easy to understand how blood could gain access to the subdural space. The pathological diagnosis was endothelioma of the dura mater.

Comment.—These so-called dural endotheliomata form a fairly common and important group of tumours. They occur in two main forms:

1. A perivascular endothelioma.
2. A psammoma in which small perivascular units undergo hyalinosis and calcification. The tumours are usually single and may be as large as a hen's egg. They first appear as flat elevations on the inner side of the dura and slowly enlarge, causing displacement or atrophy of the brain substance. They do not form adhesions but may be surrounded by a vascular capsule. The chief sites at which they are found, are the dura, over the convexity, in the falx and tentorium, and along the basal vessels. They occasionally occur over the medulla and down the cord.

Microscopically these tumours are composed of cells which are usually large and more or less flattened, but are sometimes spindle-shaped. These cells are arranged in concentric manner about strands of connective tissue or blood vessels, and form the characteristic "whorls". Occasionally a palisade effect is produced by an orderly grouping of nuclei in parallel columns.

Recently Mallory¹ has called in question the endothelial origin of these tumours. Indeed he demonstrated that there is no endothelial lining to the dura mater, which is bare except for fibroblasts. He would therefore call such tumours "arachnoid fibroblastoma."

Xanthochromia, or yellow colouration of the cerebrospinal fluid, may occur after hæmorrhage has taken place into the ventricles or subarachnoid space. Such hæmorrhages often result from a tumour in contact with the meninges or ependyma of the ventricles, and usually represent a capillary oozing. The red blood cells may be present in the fluid, or they may have entirely disappeared, or shadowy and crenated forms may be present, depending on the degree of hæmolysis that has taken place. There is always a positive reaction for hæmoglobin though the fluid may be clear yellow or slightly turbid. Globulin is present but spontaneous coagulation does not occur. The case I have just reported belongs to this type of xanthochromia, which is not very uncommon.

Probably more common and important is the group of cases which conform to the so-called Froin's syndrome in which the fluid is clear yellow, contains a large amount of globulin and coagulates spontaneously. Pleocytosis may be present but hæmoglobin cannot be detected either chemically or spectroscopically in the fluid. This is a "compression syndrome," which occurs as a result of stagnation of the cerebrospinal fluid in a lumbar cul-de-sac. The yellow colour is probably due to vascular changes which allow of a transudation of blood plasma into the sac. There is still a third variety called Nonne's syndrome in which there is a large amount of globulin but no increase in the cells of cerebro-spinal fluid. The significance of this variation is not known. Finally in intracranial hæmorrhage in the new-born Dr. Sharp² found that hæmorrhagic or yellow spinal fluid was obtained in ten cases out of a hundred normal deliveries. Of these ten cases, six showed xanthochromia without red blood cells, and he believes that yellow fluid obtained within forty-eight hours of birth, is due to transudation of blood plasma produced by venous congestion or partial asphyxia. Where minute hæmorrhages occur as a result of lacerations red blood cells are added to the picture.

I wish to acknowledge my indebtedness to Dr. Lawrence Rhea, our pathologist, for his interest and help in this case.

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THE POTENCY OF TINCTURES OF DIGITALIS AND STROPHANTHUS PURCHASED AT VARIOUS POINTS ON THE CANADIAN MARKET

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DIGITALIS: According to the instructions of the British Pharmacopoeia, tincture of digitalis is prepared by percolation with seventy per cent alcohol, from dried digitalis leaves that have been powdered to pass No. 20 mesh. The quantity of powder and the volume of alcohol to be used are definitely laid down. The powder is directed to be prepared from dried leaves of *digitalis purpurea* that have been collected from plants just commencing to flower, and dried at a low temperature and kept in well filled, air-tight containers.

According to the instructions of the United States Pharmacopoeia, tincture of digitalis is prepared from powdered digitalis leaves passing a No. 60 mesh by percolation with a mixture of three volumes of alcohol and one volume of water. The quantity of alcohol, water and powdered leaves are definitely stated. The powder must be prepared from the leaves of *digitalis purpurea* which shall not contain more than two per cent of stems, flowers or other foreign matter. If this tincture is assayed biologically, the minimum lethal dose for each gram weight of frog must not be greater than .006 mil (.006 c.c. or .090 minims) of tincture.

The British Pharmacopoeia makes no attempt to ensure that the various samples of tinctures put out by different manufacturers, and prepared under different conditions at different times shall be of the same potency, other than by stating how much powdered leaves shall be used and how much alcohol of a certain strength shall be used for the percolation carried out in a certain manner.

The activity of digitalis leaves is due to a number of glucosides, the most important of which is digitoxin. While this glucoside is the most important, it has been found by many workers that the strength of a tincture of digitalis assayed biologically, does not run parallel to the digitoxin content determined by chemical assay.

It has been pointed out by various workers that leaves vary considerably in potency. Leaves collected before flowering differ in strength from

those collected after flowering. Leaves from one year old plants, vary in potency from leaves of two year old plants. Leaves from plants grown in one locality differ in potency from leaves collected in another. Leaves from wild plants are more toxic than those from cultivated plants. Sunlight has very little or no effect on the potency of the leaves. Weather conditions according to one worker, make a difference; rainy weather before collecting the leaves appearing to lower the potency.

A very important factor in the potency of the leaves is the way in which they are collected and preserved. If collected and dried quickly to a minimum moisture content and stored in air-tight containers, the leaves retain their potency very much longer, but undried leaves rapidly deteriorate owing to the enzymes contained in the leaves breaking up and destroying the glucosides. Moist leaves are more easily destroyed by attacks of moulds.

From these details, it is very evident that tinctures of digitalis prepared from leaves from various sources may have varying degrees of potency. Unless some means, therefore, are taken to determine the potency of the tincture, and to adjust the potency to a common standard, no two tinctures are likely to give the same physiological result. A dosage determined for a patient when using a potent tincture would prove useless if a new tincture were used, which had only half the potency of the tincture first employed. Likewise a dosage determined on a tincture of low potency might lead to disastrous results if the next tincture was one of high potency.

Drugs of this class, such as digitalis, strophanthus and squills, and other drugs such as pituitrin, ergot, etc., cannot be assayed by chemical means, and recourse must be had to what is known as a physiological assay, *i.e.*, testing the action of the drug on certain animals, or animal organs. By this type of assay certain physiological reactions are made use of in order to determine the potency of the drug.

Owing to the biological variation in the reaction

of an organ or animal, this method of assay cannot attempt to approach in accuracy that attained by chemical assay. The magnitude of the error varies with the drug to be tested and also with the method used. This difficulty is partly compensated by two factors. The error of the method is by no means as great as the variation of the various specimens of the drug, and by means of the results obtained it is possible to keep the variation of the potency of the drug down within certain definite values. Another thing to be taken into account is the fact that after a certain accuracy has been obtained, further accuracy is of much less significance, due to biological variation of the patients. One patient varies in his reaction to a drug from the reaction of another patient. The state of health of a patient influences the reaction of a drug. The weight and sex of the patient has an important bearing. The normal biological variation of members of the same species towards the action of the drug may also come into play. These factors it is impossible for the physician to estimate absolutely; due allowance must be determined in each individual case. However, the biological assay has the advantage of actually measuring the effect desired when using the drug.

Method of Standardization.—Various methods have been evolved by various workers to determine the potency of digitalis. The lethal dose of digitalis tinctures for guinea pigs has been used by some workers; others have tried the lethal dose for mice. Two of the most satisfactory methods evolved up to date have been the cat method of Hatcher and the frog method, the result of the labours of various workers.

The choice of a method is determined by several factors. The cost of obtaining animals is a consideration. The laws regarding animal experimentation are important in some places. The ease with which animals can be obtained, must also be considered. The ease of manipulation and the necessary assistance, obtainable skilled and unskilled, have also an important bearing in making choice of the method.

The method used in this series of experiments was the frog method. It was found by the early workers with this method, that a lethal dose for one frog of any one tincture of digitalis would be a lethal dose for other frogs of the same weight. It was further found that frogs of different weights within certain limits, would be killed by a tincture provided the amount of the tincture was in proportion to the weights of the frogs.

Certain details are necessary to be observed in order to obtain success by this method. The frogs in successive experiments must be kept at the same temperature, since increasing the temperature lowers the amount of tincture necessary to kill the frog. Frogs of the same species must be used. Provided it is not during the spawning season, the sex of the frog does not matter materially. Frogs are found to vary according to the season of the year in regard to the amount necessary for a lethal dose. The lethal dose in summer is quite different from the lethal dose in winter.

The method of procedure is, in general, as follows: The frogs are weighed out and put into a moist incubator maintained at 21° C. They are left there for a time until they acquire the temperature of the incubator, then calculated amounts of digitalis tincture are injected into the ventral lymph sac, and the frog returned to the incubator and left for a definite time. At the expiration of the time, the frog is removed, pithed and opened and the heart examined. If the heart has stopped in systole, the result is regarded as positive. In the first series, the quantities cover a wide range of the amount of tincture per gramme weight of frog. After the range has been determined within which the lethal dose lies, the experiment is repeated and the amount per gramme weight of frog determined which is just necessary to produce stoppage of the heart in systole.

The time that the frog is in the incubator after the injection is an important factor. Some workers have made this time one hour, and others use a twelve hour period. The one hour period for some types of tinctures has been found unsatisfactory, but not for others. Owing to some undetermined factor, some tinctures do not absorb readily and the absorption is incomplete in the one hour period. The twelve hour period is rather difficult to arrange within ordinary working hours. During the course of this work, a three hour period has been used for digitalis. The section of the League of Nations dealing with standardization of drugs has recently published the report of the committee in which they are now recommending a four hour period. In their previous report they recommended the investigation of the one hour and twelve hour period and suggested that an intermediate period might be tried.

Assay of Samples on the Canadian Market.—Representative samples of various manufacturers were collected from various cities throughout the

country in the open market. These manufacturers have been designated by letters in the table below.

The United States Pharmacopœia defines a standard tincture of digitalis as one which has a potency of such a strength that .006 c.c. (.006 mil. or .09 minims) of the tincture per gramme weight of frog, just produces stoppage of the heart in systole. The following results obtained are reported in terms of the percentage of this U.S.P. standard; that is to say, if .006 c.c. of the tincture is exactly the lethal dose per gramme weight of frog, it is called 100% standard. If it requires .012 c.c. per gramme weight of frog then it is only fifty per cent standard. If it requires .003 c.c. per gramme weight of frog it is 200% standard.

TINCTURE OF DIGITALIS		
Manufacturer*		Per Cent Standard Strength
A		65%
B		150%
C		75%
D		70%
E		75%
F	1	65%
	2	75%
	3	30%
G	1	50%
	2	40%
	3	35%
	4	85%
H	1	65%
	2	75%
	3	330%†
	4	133%
I	1	75%
	2	80%
	3	80%
J	1	85%
	2	120%
	3	60%
	4	85%
	5	100%
	6	150%

*Manufacturers' names are not given.

†This sample was a concentrated sample represented to be four times the usual strength.

Discussion of Digitalis Assay.—It can be seen from these results what a wide variation there is in the potency of the tinctures offered for sale on the Canadian market. Samples of tinctures of digitalis vary in potency from a point seventy per cent below the standard of the United States Pharmacopœia, to a point 230% above the same standard; that is, some samples are ten times as strong as others. This variation is between samples put out by two different manufacturers. But the samples of the same manufacturer vary; one sample has not been found as strong as another sample purchased elsewhere or at a different time.

It should be observed that some manufacturers put out samples that are four times the strength

ordinarily used. This is marked on the bottle and should be looked for before using the sample.

It will thus be seen, that in the absence of any biological assay, how very dangerous it may be for a physician to treat a patient with one preparation of a certain batch and then to change to a different batch preparation by the same manufacturer, or to a preparation of another manufacturer, without exercising care in finding out what the dose should be under the conditions of change.

Strophanthus.—According to the British Pharmacopœia, tincture of strophanthus is prepared from a No. 30 powder of dried strophanthus seeds; these are first extracted with ether to remove fats and oils, and then treated in a percolator with seventy per cent alcohol; afterwards making up the amount to the required volume.

According to the United States Pharmacopœia, tincture of strophanthus is prepared by extracting the fats and oils from a coarse powder of strophanthus seeds with petroleum benzine and then macerating the powder for twenty-four hours and percolating with alcohol. Assayed biologically this tincture should be adjusted so that a lethal dose should be not less than .000055 c.c. (.000825 minims) and not more than .000065 c.c. (.000975 minims) per gramme weight of frog. There is no biological standard given in the British Pharmacopœia, but the British Pharmaceutical Codex gives a standard of one-quarter minim to arrest the heart in systole for a frog of twenty grammes.

The activity of tincture of strophanthus is due to the glucoside strophanthin. The strophanthin content of strophanthus seeds varies between eight and ten per cent and in order to obtain tinctures having the same potency it is necessary to make a biological assay of the drug.

The method for a biological assay of this drug is similar to that of the frog method for tinctures of digitalis. The difficulties of assaying digitalis tinctures are not met with in the assay of strophanthus tinctures. The activity is due to one glucoside only, and there is not the difficulty of variable absorption from the ventral lymph sac. The time allowed for the absorption of the drug before pithing the frog is one hour, instead of the three to four hours recommended for the assay of tinctures of digitalis.

Assay of Samples on the Canadian Market.—Samples of tinctures of strophanthus were obtained in the open market from representatives of the various manufacturers in Canada. The

following table gives the relative potency of the various samples obtained. For purposes of comparison 100% represents a tincture of strophanthus that just requires .00006 c.c. per gramme weight of frog to produce stoppage of the heart in systole:

Manufacturer*		Per Cent Standard Strength
A	1	430%†
	2	135%
B	1	150%
	2	175%
C		50%
D		30%
E		17%
F		35%
G	1	110%
	2	120%
	3	85%
H		55%

*The names of the various manufacturers are not given.

†This is a concentrated sample represented as having four times the usual strength.

Discussion of Strophanthus Assay.—From these results the variation in potency of tinctures of strophanthus can be seen to run parallel to that

of digitalis. Some samples are eighty per cent below standard and others 430% above standard. The variation between manufacturers' preparations is very marked, and the variation between samples of the same manufacturer is also marked. Before using, it is necessary to observe whether the tincture is marked as concentrated or not.

General Conclusion.—From these results it must be concluded that tinctures of digitalis and strophanthus marked "B.P." as at present met with in Canada are very variable in their potency. The designation "B.P." has no other significance than that the tinctures have been prepared in a certain way and is no criterion as to their potency. The designation "U.S.P." may be some guide as to the potency, but this will depend on the reputation of the manufacturers and how honestly they have lived up to the U.S.P. standard. It is to be regretted that in no case is the standardization of these preparations as yet subject to governmental control in this or any other country.

Postural Albuminuria.—By the term postural (or orthostatic) albuminuria, Russell means nothing more than an albuminuria which develops in the upright position and ceases when the patient lies down. Many patients suffering from scarlet fever, who present no albuminuria during the period of rest in bed, develop an orthostatic albuminuria immediately after getting up. Some, at any rate, of these albuminurias persist for a considerable time, or even permanently. Some cases of recognized scarlatinal nephritis are ultimately represented by an albuminuria of the orthostatic type. Orthostatic albuminuria may follow other forms of specific infection, or even, though rarely, arise as the end-result of a mild acute nephritis of ordinary type. The proportions of serum globulin and serum albumin are not constant in cases either of orthostatic or nephritic albuminuria, and do not enable a differential diagnosis to be made. It is suggested that in many cases the orthostatic reaction is the result of slight renal damage. But cases probably exist in which the reaction is the result of mechanical causes. As

a matter of speculation, it is suggested that in these cases the albumin comes from one kidney only. Some response to posture occurs in most cases of nephritis and possibly in all forms of albuminuria. All degrees of diminution of the output of albumin during rest in bed are met with, down to the complete cessation of the typical orthostatic cases. Orthostatic albuminuria is probably of more frequent occurrence than is generally supposed. It may pass unrecognized owing to (1) the presence of a small quantity of albumin in the morning specimen of urine due to the continuance of the upright albuminuria for half an hour or so after going to bed the night before and the consequent contamination of the night's collection; (2) the cessation of albumin excretion during diuresis, even in the upright position, and (3) the cessation of albumin excretion in the sitting position. Extreme variations in the albumin output, with at times complete cessation, are therefore to be expected.—*Jour. Am. Med. Ass.*, Nov. 28, 1925.

THE USE OF NON-SPECIFIC FOREIGN PROTEIN IN THE TREATMENT OF INFLAMMATORY LESIONS IN THE FEMALE PELVIC ORGANS*

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THE frequency of infection of the female genital tract, the intractability of such infection, and the frequency of associated complications all make the treatment of such conditions a matter of the greatest possible importance, not only to the gynecologist but also to the general practitioner. That no treatment has been universally successful is evidenced by the number advocated, and while the treatment herein discussed is not original, the results obtained in a relatively large number of cases appear to warrant the reporting of them, and perhaps further trial.

The introduction by many methods of foreign substances into the body effecting a general reaction of the tissues, and frequently subsequent cure of certain pathological lesions has been a recognized treatment for centuries; in the past this would appear to have been imperfectly effected by the production of sterile abscesses, and scarification, blistering and burning, all of these resulting apparently in the subsequent absorption of proteins. Petersen's¹ admirable work gives a résumé of the development of this theory of treatment and credits Buchner (1890) with being the first to employ the treatment in a modern way. Gilbert² in 1893 treated pleurisy with beneficial results by reinjecting serum from pleuritic effusions. Wright³ in the late nineties, while treating patients with specific pneumonic vaccine, observed a cure of gonorrhoeal infection.

Schmidt and Sexel⁴ introduced the injection of milk intramuscularly in 1916, and since that time various preparations of whole milk have been employed, viz., caseosan, aolan, etc.

Proteins in these preparations apparently are rapidly split up and hydrolized by the erepsin in the tissue fluids. Observers have found little if any difference in the action of these prepared

market products and that of sterilized commercial milk.

According to Seibert⁵, the blood contains a variety of proteins normally, and the introduction into the circulation of some proteins not normally present, either intravenously or by some other path whereby digestive changes are avoided, will as a rule bring about a physiological reaction in the organism, the degree of the reaction depending on the material, and on the dosage employed. In a large series of injections of proteins and protein derivatives, it has been found that a febrile reaction of varying intensity followed in nearly all cases, the exceptions being alcohol-soluble products. The general conclusion is that it is not the protein *per se* which the cause of the pyrogenic reaction, but rather the bacterial derivatives in the product. Further, after extensive study, it was decided that the casein, sugar, salts and fat were not responsible for the reaction when milk was used.

Clarke⁶ states that the evidence of the laboratory does not coincide with the clinical results obtained, since protein, and products of protein breakdown, and products of destroyed body cells all produce a similar reaction. He, however, believes that the common activating principle is a product of protein decomposition, and that it is this substance which produces.

(1.) Rise in temperature with increased nitrogen metabolism; (2.) Contraction of plain muscle; (3.) Increased secretion of glands; (4.) Increased permeability of capillaries, particularly those of the liver.

His classification of proteins is interesting:—

1. Proteins purified (caseosan, etc.)
2. Mixture of proteins (milk, sera, etc.)
3. Decomposed proteins (commercial peptones.)
4. Products containing decomposed protein (with colloidal metals.)

*Read before the Montreal Medico-Chirurgical Society, February 5, 1926.

Bier⁷ holds that any measure causing a breakdown of proteins in the body, such as x-ray, radium, etc., gives the same therapeutic effect as injection of the proteins. The exact effect on the body as a whole, as well as on the pathological lesions, is still problematical, but Petersen favours the theory of cellular stimulation with an increased permeability of the cell wall. Gallera recently found changes in the immunological qualities, albumin content, surface tension and hydrogen ion concentration of blood serum after three injections of foreign protein.

Protein therapy, since its introduction into gynaecology as a therapeutic agent, has been viewed by some with skepticism but more recent study—particularly that by Professor Geo. Gellhorn⁸ has given it a place over all other subcutaneous or parenteral injections as the most potent weapon in the treatment of the infectious processes, to which the female genital tract falls prey, with the exception of syphilis and tuberculosis.

In 1923, Dr. H. M. Little suggested to me the employment of foreign protein in the treatment of pelvic infection. The earlier trials were restricted to patients in whom pelvic inflammatory disease had converted the pelvic viscera into a painful mass, the type of case in whom life is a burden, and whose condition renders her a social casualty. Later, however, the treatment was extended to include a broader group, viz., gonorrhoeal infections, acute or chronic, in any part of the genital tract, as well as infections of uncertain types following parturition, abortion, curettage, etc.

Four forms of protein therapy have been employed:—

1. Blood (heterogeneous) (intramuscularly).
2. Milk (sterilized) (intramuscularly).
3. Turpentine instillation into the Fallopian tubes.
4. Actual cautery of the cervix.

The injection of blood intramuscularly was employed in but a few cases, as the difficulty of obtaining Wassermann negative blood in a large clinic, apart from being inconvenient, complicated the procedure. Moreover, the cases in which blood was used did not, apparently, improve so rapidly as similar cases in which milk injections were given.

Since 1923 approximately 300 cases, both public and private, have been given protein injections,

and of these, the first one hundred completed cases have been studied and tabulated.

Technique.—Commercial milk is sterilized in a water bath for 10 minutes, the usual aseptic precautions being taken.

The area selected for injection, in preference to the gluteal region, is situated a handsbreadth below the crest of the ilium in the mid-axillary line, because here the superior gluteal nerve is the only one possible to be injured, while in the buttock the nerve supply is more abundant, and therefore there is a greater possibility of injury, and further, the movement of the gluteus medius is definitely less than that of the gluteus maximus. These factors minimize pain and inconvenience to patients receiving deep injections.

The initial dose is 4 c.c. In the subsequent one this amount may be increased. Subsequently 6 to 10 c.c. are given. Injection is made as deeply as possible, withdrawing the plunger to make sure that a vein has not been entered. Gellhorn and others recommend the larger dosage from the start. Injections every five days have apparently given the best results, but they may be administered as often as every four days or at intervals of seven days.

The immediate result is a sharp pain (local) at the site of injection, passing off in three to five minutes, and relieved by flexing the thigh. General systemic reaction begins in from three-quarters to one and a half hours; in which the temperature may reach from 101° to 104° in six to eight hours; rigors rarely occur, and vomiting still more rarely; though headache is an almost constant symptom. Some pain may persist locally for three or four days. The formation of a small mass at the site of injection is not infrequent, but it gradually disappears within two days without any evidence of suppuration. At the site of the lesion in the pelvis, there is a dull throbbing or cramp-like pain (focal) radiating down one or both legs, and usually lasting twelve hours from the time of the injection. The whole cycle occupies twenty-four hours or less. Some patients have remained in bed two days, but this is probably due to an exaggeration of the symptoms. There were a few patients, on the other hand, who never gave a reaction, yet in these the lesion improved as much as in those responding with marked febrile symptoms. The result with a single injection has been that in every case, after

the fever has subsided, pain has completely disappeared from the pelvis, followed by a general feeling of well being.

As with the exact dose to be given, it is also a problem as to how many doses should be given. In the majority of cases the numbers of injections were usually from six to ten, although in some cases as many as twenty-two injections were administered, but comparatively little improvement in the majority of these was obtained after the tenth dose.

A phenomenon noted occasionally was conjunctival hyperæmia, which appeared in several patients, in five to ten minutes following injection. This should be regarded as a warning that the treatment should be discontinued. In one case anaphylaxis was observed in a married woman aged twenty-three years with double pelvic inflammatory disease and fixation of the uterus. After each injection the conjunctival hyperæmia became more marked, the face became flushed and with the last injection œdema of the eyelids, lips and tongue set in and she became unrecognizable. The pulse became rapid and thready; there was a marked rigor and the temperature rose to 101° within fifteen minutes of the injection. Solution of adrenalin was given intramuscularly. The patient walked home within an hour but the usual symptoms of a severe protein reaction followed. After this, in her case protein therapy was discontinued. Had this been done when conjunctival hyperæmia first became apparent, these severe symptoms would have been averted.

Abscess at the site of injection was seen only in one case and it was with the twenty-second injection.

The symptoms may vary with each injection in the same individual even though milk presumably of the same standard is employed. "Top milk" of the commercial variety gives an increased reaction. The explanation does not appear to lie in the increased fat content, as it has been conclusively proven by Petersen and others but in that increased bacterial metabolic products harbour in top milk. The reaction following top milk is extremely painful locally, and all symptoms are intensified. This is also apt to be the case when an injection follows closely on a heavy meal.

If after six to eight injections the pelvic mass does not become progressively smaller, the treatment should be suspended for a time, possibly

for six months, or longer if the patient does not complain of abdominal pain, arthralgia or increasing debility.

The electric cautery was found to give beneficial results, particularly in broad ligament infections following abortion. The cervix should be deeply cauterized, using a small point and inserting it deeply into the canal wall at several points and allowing it to remain from eight to ten seconds with each puncture. On the following day the patient may complain of general malaise, with slight pain in the focal lesion, and a temperature from 99° to 100°. Marked improvement has followed. The reaction was much the same as with milk but the symptoms were less severe.

Illustrative case.—Mrs. S. with gonorrhœal urethritis and endocervicitis was pregnant two months. She was given injections of milk twice with little improvement. Abortion took place at three months (evidently induced). She then consulted another doctor and was curetted. She returned in six weeks with a post-partum mass in the right quadrant of the pelvis. The uterus was fixed, the cervix thick, granular and everted. This was cauterized on three occasions at six-day intervals, and as an apparent result the mass disappeared completely, the cervix became normal, the uterus movable, and all the symptoms cleared up. Incidentally, all evidence of the urethritis also disappeared. Undoubtedly the same principle applies here, and if it be true that the action of foreign protein on the lymphatic wall is the essential factor, then this method, acting directly on the lymphatics of the broad ligament of the pelvis, is a direct injection into the infected part. Four other cases were cauterized, all of whom showed equal improvement.

Contraindications.—So far as is known there are but few contraindications to the administration of foreign protein. Menstruation is not considered a contraindication, the patient receiving her injection on the scheduled day even while menstruating. Lux and other writers state that protein injection augments the menstrual flow.

During pregnancy the employment of foreign protein has always been regarded as questionable, particularly in early pregnancy and at or about the time of the menstrual period. However, four cases were given milk in this way and none aborted, although one case at three

months had uterine contractions for a few hours, followed on the next day by "spotting." One case came to the clinic late in the eighth month with an acute gonorrhœal infection. Routine treatment was carried out in the clinic and subsequently by her physician. Labour came on at the expected date, and recovery was uneventful. At no time subsequent to labour were there any symptoms (leukorrhœa, etc.) nor were any gonococci isolated.

One diabetic was treated in this way for double pelvic inflammatory disease; the reaction was intense but the therapeutic effect most striking. The patient was kept on diabetic diet and under the strictest observation, but no untoward effects resulted. Six months later she complained of pain in the lower abdomen. An exploratory laparotomy was made under gas and the appendix, which was long and inflamed, was removed but the tubes were found healthy and patent.

In syphilitic patients, who are under active anti-syphilitic treatment the effects of treatment are intensified by the administration of protein.

A markedly febrile condition is no contraindication to protein therapy; indeed frequently there may be an almost instantaneous return to normal temperature with disappearance of all symptoms.

There are certain contraindications to the administration of foreign protein; cases in which from experience it is obvious that no good can be obtained. The chronic long-standing case where the appendages are not involved cannot be expected to improve.

Increasing cachexia from persistent, long-standing infection is a condition to be carefully considered, and if treatment be given only small doses, 4 c.c. should be employed. If, however, the cachexia becomes more marked, treatment should be discontinued. Cachexia developing from employment in this way of foreign protein has been observed by some clinicians, but this complication has not been noted in our clinics. Foreign protein is distinctly contraindicated where there is tuberculosis in any part of the body. Patients known to be sensitive to sera should at first be given the smallest dose. Anaphylaxis fortunately is an extremely rare phenomenon, but, especially when beginning treatment, should always be borne in mind.

The end results in the hundred cases mentioned were as follows:

All were treated with a minimum number of injections, in conjunction with recognized local treatment, e.g., urethral instillations of argyrol 20 per cent, picric acid 3 per cent, applied to the cervix and cervical canal, daily douches, etc.

The results were specially encouraging in acute or subacute types, either gonorrhœal or non-gonorrhœal, involving the lower part of the genital tract. Chronic, long-standing cases of either type, in spite of more prolonged treatment, did not respond nearly so well. The acute cases showed 55 per cent of cures, with nine weeks of treatment, whilst the chronic showed only 18 per cent of cures, and this in spite of twelve weeks' treatment.

With infections involving the higher portion of the tract, whether salpingitis or tubo-ovarian infection, with so-called pelvic peritonitis, the results were about the same in each group, i.e., 44 per cent cures, 40 per cent improved, 16 per cent no change, except that tubal infections not involving the ovary required twelve weeks' treatment as against nine weeks where there was tubo-ovarian mass.

In comparing the results in treatment of chronic types, gonorrhœal or otherwise with acute or early infections, protein therapy was distinctly disappointing, there being cures in 20 per cent, unimproved in over 40 per cent, in spite of treatment for from three to four months.

The results were gratifying in that particularly difficult type of case showing post-partum pelvic lesions, laceration of the cervix and infiltration of the broad ligaments. Of these, 20 per cent were cured and 19 per cent improved in a period of only six weeks. These figures could probably have been improved on if some patients had returned more often. However, the fact that they did not is presumptive evidence of their being sufficiently relieved to carry on their family duties.

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TUBERCULOUS COMPLICATIONS IN THE DIGESTIVE TRACT MET WITH IN THE COURSE OF PULMONARY DISEASE

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WE have selected this subject for discussion for several reasons; because of the frequency and seriousness of digestive tract complications, their importance in definitely determining the prognosis, and because of our own interest in this phase of the subject. One is more and more impressed with the oft-repeated dictum of thoughtful medical writers that tuberculosis is a general disease, and that it is a mistake to think of tuberculosis as of the lung or of the joint; rather should we think of it as a disease of the man himself. In our attempt at greater accuracy in the localization of the offending focus, we sometimes leave our work half done, forgetting that we are dealing with a generally sick individual.

Beginning with the lips, the literature does not present a great array of material, but what there is leads us to think that tuberculous lesions in this area are comparatively rare; in fact, oral tuberculosis is the most uncommon of all. This condition is seen in two manifestations; solitary ulcer of the lip, the most unusual type, and ulcerated areas secondary to disease of the buccal membranes or to lupus of the face. MacPherson and Gregg¹ report a typical case of the first form. The appearance of the ulcer, partly on the mucous membrane and partly on the integument, round or oblong in shape with thickened edges lightly raised and showing a tendency to undermining, with indurated base and infiltrated and inflamed surrounding tissue, was associated with enlargement of the submaxillary and submental glands. The diagnosis was made of a tuberculous ulcer, after finding a positive, previously unrecognized pulmonary tuberculosis, and this was later confirmed by a microscopic study of a section of the ulcer. The similarity of this condition to that of a local carcinomatous or syphilitic manifestation is recognized, and in general a definite diagnosis can be made only by microscopic study. The treatment suggested is the use of a caustic (acid nitrate of mercury or galvanic cautery) or surgical removal. We would add the use of the Kronmeyer lamp, if this machine is available. The result of such treatment is excellent.

The diagnosis of the second type mentioned, in which there is an extension of a lupus is easily made. A discussion of the treatment of lupus would require much time, and we only mention the accepted modern methods: liquid acid nitrate of mercury, turpentine oil, the Kronmeyer lamp, x-ray, radium, and diathermy. Here we may introduce the recent observation of Corper and Luie² on the effect of cauterization on cutaneous tuberculous lesions, and its use in all localized tuberculous disease within its range. Cauterization of a local lesion caused by less virulent human tubercle bacilli efficiently destroys the lesion and has a beneficial, stimulating effect on the surrounding tissue, and does not tend to a systemic dissemination of the disease. When however, highly virulent bacilli exist in the tissue, the effect of the cautery is not so satisfactory locally and there is greater danger of dissemination.

In the mouth we may encounter tuberculous complications of the oral mucous membrane. These lesions may also occur in two forms, an extension of lupus and a definite localized tuberculous ulceration. According to Ivy and Appleton³, ten per cent of lupus cases show oral lesions. They are slowly progressive, with very little tendency to ulceration. The ulcerative lesion may extend in the same manner as those found in other tissues, and involve tongue, gums, hard and soft palate. They are usually irregular in shape, and slightly undermined; not, as a rule, deep, with little induration; the surfaces are granular, covered with reddish or yellowish points and yellow streaks; and there is a fairly constant tendency to grow worse. They are almost always secondary. The diagnosis is dependent upon the above points; but should demand also sputum and tissue examination, and an animal inoculation test; pain is a distinct feature.

The treatment for the primary form is general and local. The latter consists of curetting followed by cauterization and the use of one of the chlorine compounds as a mouth wash. As we have stated above, these complications are relatively rare. The following is a report of the only case

we have seen in nearly two thousand tuberculous individuals.

A patient suffering from far advanced pulmonary tuberculosis, whose sputum was laden with bacilli, noticed a tender spot on the tip of the tongue. He was fearful of cancer, and therefore presented himself early. Examination demonstrated a crack in the surface of the tongue, approximately one-quarter of an inch in depth, the edges of which were pale and anæmic in appearance and slightly elevated. There was practically no induration. The crack was covered with a few yellowish strands and raised reddish areas. The diagnosis was confirmed by microscopic examination after removal of a small section. Treatment, in nearly all cases, has been satisfactory, provided the patient's general condition warrants a favourable prognosis.

The tonsils come within reach of tuberculous infection, and during the last few years much attention is being paid to these possible offenders. Weller⁴, in his examination of 8,697 sectioned tonsils, found 2.35 per cent with tuberculous lesions. MacCready and Crow⁵ believe that nearly five per cent of tonsillar infections are tuberculous. Fisher⁶ further claims that in 73.2 per cent of the patients, who have ulcerative tuberculosis of the lungs and who die, involvement of the tonsils may be demonstrated. Three types are recognized: local crypt infections; ulcerative, lupus-like lesions; and miliary tuberculosis. The infection of a crypt is the most common. It is usually unilateral, involving one or more crypts and avoiding the lymph follicles. It is felt that these lesions are mainly primary, as they occur more often in patients having no pulmonary tuberculosis. The ulcerative, lupus-like lesions usually result from a coalescence of crypt infections or from extension from surrounding areas. The last class, the miliary type, is usually bilateral, and can best be explained by a hæmatogenous infection. We may say that the diagnosis, in the majority of cases, has been made after removal of the tonsils, and the treatment should be left to the surgeon.

Extensive search of the literature on tuberculosis of the stomach yields but a meagre return. Broders⁷, in an interesting discussion of this condition, in 1917, states that a critical survey of the literature disclosed forty-nine cases which may be considered as definitely tuberculous, one hundred and eighteen as probably tuberculous, fifty-nine as doubtful, and eighty negative. Of the forty-nine tuberculous, thirty-three were adults, with about equal division between the sexes. In forty of them ulcers were found, fourteen being single and nineteen multiple. The remainder were associated with miliary tuberculosis. The predominating site was the lesser curvature, followed by the greater curvature, the pylorus, and the pos-

terior wall, in the order named. Thirty-four cases were associated with pulmonary disease, and twenty-nine had intestinal involvement. He believes that only two cases could properly be called primary. A recital of his one case may be of interest as it is quite typical of the others.

A man, forty-two years of age, had had local symptoms in the stomach for over two years. An exploratory operation was done by a surgeon, and a diagnosis of inoperable carcinoma made. Symptoms were heaviness in the epigastrium, severe vomiting immediately after meals, regurgitation and emaciation. Neither pain nor hyperacidity was present, but the patient complained of excessive hunger. The roentgenological report was operable carcinoma. At operation, two-thirds of the stomach was removed. A tumour was found near the pylorus. There was marked spasm of the musculature throughout, but no dilatation. The lesion itself consisted of three ulcers with ragged edges and dirty grey bases. Microscopic examination revealed typical ulcerating tubercles. Autopsy gave further illumination in the way of a considerable area of fibro-caseous disease in the lungs.

Razzaboni⁸ reports a case in a woman of sixty who recovered after a sub-total gastrectomy. Baetzner⁹ cites a recent case, and mentions, among the symptoms, severe pain one-half hour after meals, absence of hydrochloric acid, presence of occult blood, and lactic acid. All authors who have successfully operated upon their patients mention the later formation of extensive adhesions and advise gastro-enterotomy. It can readily be seen that tuberculosis of the stomach is extremely rare; that diagnosis cannot be definitely made from symptoms alone; that x-ray examination adds nothing of importance; and that exploratory incision alone can determine the cause, and incidentally the only cure mentioned at the present time appears to be surgical removal.

Tuberculosis of the liver is not a common condition, except in general miliary tuberculosis. Of the latter we will not speak, but rather of the isolated case with abscess formation. Several authors, especially Gerlach¹⁰ and Vemming²⁵ have given this condition critical study. The latter have practically covered the ground. They mention the important fact that in thirteen cases the first clinical manifestation was a gravity abscess in the sheath of the right rectus muscle, secondary to a subphrenic abscess which in turn could be traced to a perforated tuberculous process in the right lobe of the liver. The whole diseased area shelled out readily after the ligation of the larger vessels. The literature reveals some twenty-nine cases in which operative treatment was successful; in nineteen of these, irritation of the surrounding tissues occurred, or rapidly formed pus caused distension of Glisson's cap-

sule. In the remaining cases localized symptoms were preceded by fever, severe sweating, and loss of weight, strength and appetite.

The influence of disease in the intestinal tract on the course of pulmonary disease has long been known. No clear differentiation has been made between gastrointestinal symptoms referable to the general toxæmia of the pulmonary disease and those due to involvement of the tract itself. We were taught to expect from tuberculous enteritis and colitis definite symptoms—pain, diarrhoea, rapid emaciation, etc. But now we have learned how far off the right track we were. More recent diagnostic methods and more careful observations have given us a new conception of this dreaded complication; new light has been thrown upon more satisfactory treatment, and the prognosis, which has hitherto been considered most gloomy, is now more cheerful. The literature amassed on this subject is extensive, and certain names stand out prominently. Steirlin in Germany¹¹, Beclere and Merial in France¹², Archibald and Pirie¹³, Pritchard and Stewart in Canada¹⁴, Brown, Sampson and Heise¹⁵, and Carman¹⁶, in the United States. The frequency of this complication has been variously estimated from four to five per cent in minimal pulmonary disease to between sixty and ninety per cent in severe fatal cases. Stewart makes a conservative estimate of eighteen per cent of all groups; a more likely figure would be 15-20 per cent, approximately the same percentage as that estimated for the occurrence of tuberculous laryngeal complication. Our own observation leads us to believe that the last figure would be the more accurate. Of seventeen apparently hopeless cases observed last year, all but one are now dead.

A controversy has arisen concerning the mode of infection; is it hæmatogenous or by penetration from the intestinal tract? Archibald believes in the hæmatogenous origin, but infection from inside the tract does occur, and that not infrequently.

A few words concerning the pathology: Two main classes are distinguished, ulcerative and hypertrophic. The former is largely a process of destruction, either acute or chronic. The breaking down of the tubercle usually takes place in the submucosa, proceeding to softening and final destruction of the mucosa, and setting up a small area of reaction, found only in serial section. The latter, a purely hypertrophic reaction of the tissue, is of productive nature, and tumour masses are found. Repair and destruction are associated

with this type, and more or less stricture is noted. Archibald¹⁰ recognizes the presence of tubercles during operation by a slight nodular thickening, cedema of the wall, loss of elasticity, and a rosette of capillary congestion opposite the tubercle in the peritoneum, with a patch of fibrinoplastic exudate forming a thin veil.

Careful history-taking and diagnosis of patients coming for treatment of pulmonary tuberculosis will reveal in nearly all cases certain gastro-intestinal disturbances, all the way from anorexia to severe diarrhoea. Just where are we to draw the line and decide that the patient has a definite tuberculous enteritis, appendicitis or colitis? Stewart feels that many cases have no gastrointestinal symptoms whatever. This has been confirmed by Heise, Brown, and Schwatt²². In all probability the majority of these cases are very early. The first symptom of a definite entero-colitis, mentioned by many authors, is that of an excessive nervous irritability. This seems to be a very early one; but a great deal of care must be taken in its interpretation, as later experience demonstrates that many have this irritability without intestinal disease. Anorexia is another symptom often mentioned, and abdominal discomfort associated with nausea. Definite pain is a frequent symptom. Archibald observes that pain below the umbilicus coming on at irregular intervals during the day, but occurring chiefly from the late afternoon on, is characteristic. Some observers have noted the greatest distress from three to four o'clock in the morning lasting until after breakfast with pains crampy or stabbing suggesting gas pains. These pains are intensified by food and relieved by fasting, and occur generally during only part of the day but persist day after day. Constipation, so common as a result of the sedentary life of these patients, is met with as a frequent symptom of enteritis; and is a symptom to which it is difficult to give due significance; obstinate constipation should always lead to suspicion. Diarrhoea, next to pain, is the most common symptom, but caution must be exercised in passing judgment on its occurrence. A patient who has formerly been constipated may tell you with delight that now he has more than one free movement daily without the use of a cathartic; this fact alone should lead you to be suspicious. A condition of alternating constipation and soft stools must not be overlooked. We would add an observation of our own which seems to us of importance. Usually, all patients coming to the institution are kept in bed, and most of

them gain weight at this time. Failure to gain weight under these conditions without any advance of the pulmonary disease or notable increase in its activity, is very suspicious of an intestinal complication; especially is this so if associated with a slight rise of temperature. Furthermore, when a patient gains for the first month or so, and then begins to lose a pound or more a week without a change for the worse in his pulmonary condition, we should investigate thoroughly the condition of his intestinal tract.

To recapitulate: nervousness; failure to gain in weight, or slight loss of weight in spite of treatment, without associated increase of pulmonary disease; anorexia; discomfort and pain in the lower abdomen; nausea; obstinate constipation; and finally diarrhoea, are the classical symptoms of intestinal tuberculosis, and usually follow in the order mentioned.

We attempt to check up our diagnosis by roentgenological examination with the barium meal and opaque enema, and by examination of the stools for blood, pus, and tubercle bacilli. The usual accepted procedure is simple. No cathartic is given for at least two days before the barium meal. The patient goes breakfastless on the morning of the observation. He is then given the barium in milk, buttermilk, malted milk or some such medium. We have found the most practical meal to be a glassful of thick gruel, followed by a glass of milk and one of water, each of the three containing two ounces of barium sulphate. Some observers give a preliminary barium meal at four to five o'clock in the morning, but we believe that it is best to adhere as nearly as possible to the usual meal-hours. The passage of the meal is carefully watched under the fluoroscope. The type of stomach, size of the gas bubble, filling and emptying, tone of its musculature and evenness of its contour are noted. An observation of probable value is unusual delay in the emptying of the stomach. This may be due to irritation in or around the caecum and is reflex in origin. The patient is fluoroscoped at two-hour intervals and the rate of progression of the meal noted. This is to be continued until the barium is well into the large intestine.

It seems impossible at the present time to make an accurate diagnosis of a tuberculous involvement of the small intestine by roentgenological examination. Some observers believe that the appearance of segmentation has some pathological significance, but we have seen this in normal persons. Following the barium meal to the ileo-caecal valve, we may note a delay of several

hours. This is not a positive finding but suggests irritation of the caecum or a mechanical interference with the passage of the barium into the bowel. In from three to five hours one usually finds the barium filling the caecum, and this is really the beginning of our most important observations. The pathological appearance here of prime importance is a definite filling defect which remains constant and can be verified by subsequent examination with the barium meal and enema. A ragged outline of the large intestine or a definite appearance of spasm or segmentation of the colon, particularly the caecum, is also of value. Finally, a phenomenon of considerable importance and rarely seen is that of a rapid emptying of the caecum upon manipulation by the examining hand. A great deal of care must be taken in the interpretation of a filling defect which may appear in the first third of the transverse colon. Case 17 has pointed out that in all probability, somewhere in the first third of the transverse colon, an apparent filling defect may occur, which, however, may be explained by a contraction ring from which point both peristalsis and anti-peristalsis are set up.

To sum up the importance of roentgenological examinations in the diagnosis of intestinal tuberculosis, the only positive evidence of tuberculous ulceration seems to be a definite, persistent filling defect in the large intestine when other pathological conditions that may produce filling defects are excluded. A too rapid rate of progression of the barium, or iliac stasis, or rapid emptying of the caecum on manipulation, is strongly presumptive evidence of ulceration. Because we may be deceived by the appearance of the barium meal in the transverse and descending colon, it is necessary to follow the meal by a barium enema with further fluoroscopic examination and x-ray films.

Examination of the faeces for pus, blood, and tubercle bacilli should be made, remembering, however, that a large percentage of patients who have positive sputum will show tubercle bacilli in the faeces.

We now have the evidence given by the symptomatology, the roentgenological examination, and the examination of faeces. A skilful and proper balancing of these should guide us toward a correct diagnosis of tuberculosis in the intestines.

Now as to treatment, to operate or not to operate, that is the question. Senn¹⁷ seems to have made the first complete survey of the literature in

1898, and stated that medical treatment had been inefficient and that surgery offered a little hope in an altogether hopeless field; but he felt that the prognosis of an operation depended upon the pulmonary outlook of the patient. Since then, Hemmeter²⁰, Lemon²¹, and Archibald¹⁹ have elaborated this method of treatment and the last-mentioned gives a very encouraging report of the result of operation in relatively early cases with moderate pulmonary involvement. Appendectomy, and short-circuiting are the procedures usually followed, the choice depending upon the extent of the disease found during the operation. Since Senn's time heliotherapy and ultra-violet ray therapy have been introduced: the use of insolation, Alpine sun lamps, arc lamps and their kindred. Rollier²³, who has done most for the promulgation of heliotherapy, (though his work has been mainly with glands, bones and peritonitis) has stimulated many men to the extensive use of the cheapest medicine known—sunlight. Great care must be used at first even in this source of therapy. Associated with it is a variety of aids, the most important being bed rest for long periods of time, associated with a special diet. We have found that a diet very low in fat, and with special preparation of the food to eliminate all irritating particles gives the patient the greatest comfort. Another valuable adjunct, for the suggestion of which we are indebted to Dr. C. D. Parfitt, is the daily use of the normal saline enema. It seems reasonable that the greatest possible cleanliness of the bowel will prevent absorption of intestinal toxins. For the relief of diarrhoea Saxtorph²⁴ was the first to use calcium chloride intravenously, five c.c. of a five per cent solution weekly. He has had many enthusiastic followers in this treatment, but of late it seems to be falling into some disrepute. For other symptoms, such as pain, flatulence, etc., each physician will have his own pet mixtures or means for alleviation.

In tuberculous peritonitis, we generally recognize two main types, plastic and exudative. The

former is more chronic, with a greater tendency to form adhesions, and a slower response to treatment. The latter gives rise to less trouble with adhesions but more discomfort due to the accumulation of fluid; it has also a better prognosis. Surgeons and physicians have disputed as to the best method of treatment. Both have advocates, but we believe the pendulum is swinging towards the medical side, and we think that patients who have been treated surgically should also receive the full benefits of medical treatment. Collections of fluid should be withdrawn and air or oxygen may be substituted. Rollier²³ has demonstrated excellent results from the use of sunlight and bed rest. In districts where the sun is timid about its appearance, the violet ray lamp or the arc lamp is of great help. Various other treatments have been resorted to, but we believe they are disappearing in the light of results obtained by simpler methods.

In a future paper we may have something to say on tuberculous ischio-rectal abscess.

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The Significance of Cardiac Extrasystoles in Childhood.—Three varieties of extrasystoles occurring in childhood—emotional, toxic and idiopathic—are described by Murray H. Bass, New York. Of these the toxic and the idiopathic are the most important. The toxic variety occurs in the course of, or as the result of, acute

infections. It is usually transitory and, although coincident with acute cardiac inflammation, is not necessarily an evidence of severe permanent cardiac injury. In most cases the irregularity completely disappears and does not seem to leave the child predisposed to attacks of recurrence.—*J. A. M. A.*, Feb. 6, 1926.

THE USE OF EPHEDRIN IN BRONCHIAL ASTHMA

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THERE are certain types of chronic asthmatics who require frequent relief of their paroxysms. In such cases there is no remedy which is so generally effective as is adrenalin, but it has two disadvantages: it is only effective when given hypodermically, and its action is short-lived. There is therefore more than an academic interest in establishing the claim made for the drug ephedrin, that it possesses qualities similar to those exhibited by adrenalin, with the difference that it may be effectively administered by mouth, and that the relief it produces lasts for a longer time.

Ephedrin is an alkaloid which is the active principle of the plant *Ephedra vulgaris*. Decoctions of the plant have been used in China for many centuries, for diaphoretic and antipyretic purposes, and also as a sedative in cough; and the chemistry of ephedrin has been known for many years. It is curious, however, that notwithstanding the fact that its mydriatic qualities have been recognized, and that it is absorbed promptly from the intestinal tract without change, no attempt has been made until very recently, to test its value as an antispasmodic in asthma. It has been used in Japan in a preparation named "asthatol," and has also been combined with homatropine in the compound "Mydin," but only within the last year has its use in asthma been suggested.

The pharmacology of the drug has been fully dealt with by Chen and Schmidt,¹ in connection with which there should be read an extremely suggestive paper by Barger and Dale² on the sympathomimetic effects of a group of amines including adrenalin, tyrosine and ephedrine. Certain clinical applications also have been dealt with by Miller.³

The object of the present note is to report the results obtained from the use of ephedrin in a group of cases of asthma over a period of about three months. This series comprised twenty cases of severe and recurrent bronchial asthma of ages varying from 14 to 60. Care was taken

to select only those in whom the symptoms were typical and of an acute nature, and the effects produced were gathered both by personal observation, and by close and repeated questioning.

Care was taken to observe (a) how soon effects were produced: (b) how long these lasted in comparison with adrenalin: (c) what other results there might be.

In most cases relief was obtained in from two to five minutes after swallowing a capsule. This was the case not only in different patients, but also in different attacks in the same patient. They had the same sense of relaxation in the chest as they gained from adrenalin, and in one or two instances it was found on auscultation that a notable diminution in the mass of râles was observed as occurring simultaneously with the feeling of relief; but complete disappearance of the râles is not of course a guide to the degree of relaxation of the spasm. In most cases the patient stated that there was little if any difference between the two drugs in the length of time for relief to appear. On the whole, it was found that the effect came more rapidly if the ephedrin was taken on an empty stomach.

It was quite clearly established that the ephedrin produced more lasting effects than adrenalin. In some cases the patients would pass an entire night of comfort after taking a single dose of ephedrin, or, if they had some during the day, would be able to go out walking or otherwise exert themselves without distress. In such patients adrenalin gave no more than one or two hours help. On the whole, ephedrin seemed to give protection for from six to eight hours.

As regards other effects. The blood pressure was not found to be appreciably altered by the dose requisite to give relief. Readings before and after administration were taken in five cases, over a space of twenty minutes to half an hour, and in no instance were there more than two

or three degrees elevation as a result. In two cases there were pronounced feelings of quivering and nervousness, which, however, passed off within an hour or less. Headache, thirstiness and giddiness, were other transient effects noted.

The dosage required some regulation. In some cases, 25 mgm. was found to be quite sufficient: 50 mgm. in these patients gave rise to the disagreeable effects mentioned. Other patients needed 50 mgms. for effects, either taken at once or in two separate capsules. Dosage can best be judged by beginning with 25 mgms. and increasing if required.

The conclusion to be drawn from these experiences is that ephedrin produces well-marked antispasmodic effects in asthma: that these are of longer duration than those produced by adrenalin in similar cases, and that repeated doses may be safely given over prolonged periods.

My thanks are due to Dr. R. L. Stehle, of McGill University, for a supply of the drug.

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Hexylresorcinol in Infection of the Urinary Tract.—In the treatment of practically every type of urinary infection with hexylresorcinol, Damon A. Brown, Wis., has found relief of vesical irritability to be the outstanding result. In most cases, frequent urination, burning and tenesmus are completely relieved. Many of the sixty-one patients reported on had been treated with other forms of therapy without result. Approximately 50 per cent of the patients in this series had had gastro-intestinal disturbances, varying from slight gastric distress to severe bloating, belching, nausea, vomiting and diarrhea. Brown suggests that perhaps these disturbances have been due as much to the oil in which the drug is suspended as to the drug itself. Practically all patients who had such difficulty did not digest fats easily and were generally subject to more or less gastric distress and constipation. The site of infection in the urinary tract was: upper, two cases; lower, thirty-eight cases; upper and lower, twenty-three cases. Complications included ureteral stricture with hydronephrosis, vesical and ureteral calculi, hypertrophied prostate, bladder diverticuli, and vesical neck contracture. Appropriate treatment was instituted in all these conditions. Of the three cases which showed no clinical improvement and in which the pus content and cultural findings of the urine remained unchanged, two were due to severe *B. coli* infections of the prostate and seminal vesicles complicating gonorrhea. The other case occurred in a frail elderly man with a marked

vesical neck contracture, chronic, purulent cystitis, and bilateral pyonephrosis due to staphylococcal infection. Two patients with tuberculous cystitis remaining after nephrectomy and ureterectomy were considerably relieved of tenesmus and frequent urination while taking the drug. The average daily dose of the drug was from nine to twelve capsules. Each capsule contains 0.15 gm. of hexylresorcinol. The dose was determined by the patient's tolerance and the virulence of the infection. Without question, the higher the concentration of the drug in the urine, the quicker and more complete is the therapeutic effect. In the acute cases, most of which were due to staphylococcal infections, treatment was continued from seven to thirty days. Although the drug was given for an average of from thirty to sixty days in most of the chronic cases, it was necessary to prolong treatment for four or five months in a few very resistant infections. Brown says that types of infection in which beneficial results cannot be expected are (1) infections of the kidney, (2) renal and bladder tuberculosis, (3) infections of the prostate and seminal vesicles, and (4) gonorrheal urethritis. In infections of the renal substance, the prostate and the seminal vesicles, the drug is not brought in contact with the offending bacteria in sufficient concentration or for sufficient length of time to have an inhibitory or lethal effect. Also, urine containing the drug does not come in contact with invading organisms in the urethra for a sufficient length of time to exert a bactericidal effect. *Jour. Am. Med. Ass.* Mar. 6, 1926.

Case Reports

TRACHEAL COLLAPSE DURING THYROIDECTOMY

BY CHARLES K. P. HENRY, M.D.

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The knowledge of complications commonly occurring during operative procedures is essential to every surgeon. When a complication occurs but rarely and requires some special measure to combat it, especially if it imperils life, or causes death if not overcome quickly, a surgeon should have the knowledge to promptly recognize it and also properly deal with it.

Collapse of the trachea during thyroidectomies is a rare occurrence, but all the more serious because of this rarity. During the last fifty years the mortality in goitre operations has decreased till now, in the hands of expert operators, it is almost negligible in non-toxic cases, and is only from two to five per cent in toxic cases. Rose in 1878 called attention to the importance of tracheal compression and the possibility of asphyxia from obstruction due to this cause. There are a few cases where increasing cyanosis occurs after operation and dyspnoea increases and death results in the first twenty-four hours after operation. No such cases have come to our notice at the Montreal General Hospital to date. They are not likely to arise from laryngeal injury, as apparently in humans both nerves may be injured or divided without producing serious dyspnoea, cyanosis or death. Frey¹ has stated that immediate death in a dog from double inferior laryngeal nerve section has never been reported. Experiments in dogs have shown that when sufficient cartilaginous rings have been removed there may result a progressively increasing inspiratory stridor which would have resulted in death had not a whalebone catheter been inserted through the larynx. If the mucous membrane of the trachea were incised the dog became dyspnoeic at once with inspiratory stridor and increase in tracheal collapse. Suture closure immediately relieved the symptoms.

Our case had no injury to her recurrent nerves, her voice was unimpaired, she had no laceration of her trachea, muscular or mucous layers, she had no cough, expectoration or blood expectorated. She had tracheal narrowing as shown by the x-ray prior to operation. As far as can be

decided she suffered from sudden tracheal occlusion. The history of her case is as follows:

Mrs. F. W., aged twenty-eight, case No. 3,598, was admitted to "L" surgical service, Montreal General Hospital, August 1, 1924, and was discharged August 27. She presented the classical symptoms of Graves' disease, exophthalmos, tachycardia, increased blood pressure—160 systolic, 80 diastolic—nervousness and a basal metabolic rate of plus 77 two days before admission.

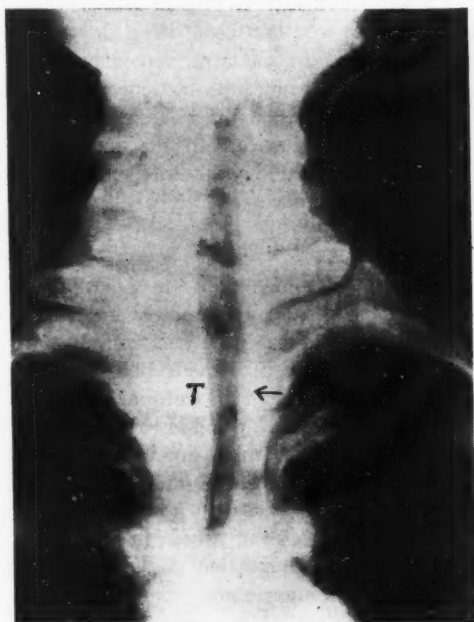
X-ray examination showed "right sided compression of the tracheal shadow and displacement of the trachea to the left." Laryngeal examination was normal, and there was no enlargement of the lingual tonsil. She was prepared in the usual way, and six days after admission her metabolic rate had fallen to plus 42. Operation was done on August 11, under local anaesthesia, novocain 2% for skin and 1½% for deeper structures. On beginning operation her pulse was 180 but it fell to 100, and the subtotal thyroidectomy was readily performed with absolutely no complaint or evidence of discomfort from the patient. Part of the operation report is quoted *verbatim*:

"Closure was exceptionally easy and rapid.

During the application of the dressing and bandage, the patient, who had previously had no trouble with respiration, whose phonation was normal, who had no cough, vomiting or mucus in her throat, suddenly began to suffer from obstructive breathing. Her respirations became more difficult, evidently she was not getting air into her lungs, and she became deeply cyanosed. She got to the stage of deep narcosis, with beginning convulsive movements and was unconscious."

The intra-tracheal tube was rapidly passed by the anaesthetist, Dr. C. C. Stewart, who was in the next theatre, and her colour and breathing became normal, and she became conscious. Her pulse was unaltered and remained good even when she was deeply cyanosed. The tube was left in for fifteen minutes, when she stated she felt quite well, so it was withdrawn. The condition immediately returned, and the tube was re-introduced. She was left in the operating room for an hour, and was given the usual post-operative, intravenous, glucose saline. Her dressing was changed, there was little oozing, remarkably little

for so much handling, and there was no hæmatoma or swelling of the neck. She went to her ward, pulse 96, respirations 24, and she was able to talk with the tube *in situ*. She swallowed water and the tube caused no gagging. It was removed twenty-four hours after operation, and the patient made a good recovery. She was discharged in sixteen days. In two weeks her metabolic rate had dropped to plus 10. Twelve hours after the tube was inserted mucus in throat was cleared by suction apparatus. She had no more tracheitis, cough or mucus than the average case. Her voice remained unaltered.



Photograph from x-ray plate which shows the narrowed trachea at point T.

Considering the flattened trachea, as shown by x-rays, I believe this collapsed when the dressing and bandage were applied. She had then complete tracheal compression, and without a tracheotomy or an intra-tracheal tube she would have died immediately. The internal splinting of the weakened trachea by our tube for twenty-four hours enabled it to remain open afterwards.

Two months after discharge from hospital her rate was minus 3, a fall from plus 77 before admission. She had lost her tremor and her exophthalmos was much less. About three months later she returned to the goitre clinic. She had gained twenty pounds, was less nervous, was sleeping well and feeling better than she had for some years.

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A CASE OF OBSTINATE URETHRAL AND RECTAL RETENTION CURED BY PSYCHO-ANALYTIC METHODS

By N. VINER, M.D.

Montreal

Miss J. H. twenty-five years old, came to the gynaecological clinic of the Montreal General Hospital in October, 1923, complaining of pain in the left lower inguinal region and profuse bleeding at the menses. She gave a history of a previous gynaecological operation, which turned out to be the removal of her left tube and ovary three years before. Her menses which had started at ten and a half years, and recurred every four weeks, lasted ten to twelve days, until eight months before when they began to persist for from fifteen to eighteen days, and to be very profuse and accompanied by clots. There was also a moderate degree of leucorrhœa. The general health and condition were only fair; there was nothing else of interest, except that she urinated only once or twice a day and not at all at night.

An examination under gas anaesthesia, on November 1st, by Dr. Patrick, showed an intact hymen, a small, retroverted uterus and a small tight cervix. A similar examination on December 8th after her admission to the ward, showed nothing new. A laparotomy on the same day showed the same findings as above, plus the absence of the left tube and ovary from a previous operation and the right ovary somewhat enlarged and accompanied by a small cyst: A ventral suspension was performed (suturing the uterus to the peritoneum with double sutures), and the abdomen was closed. During the following twelve days the patient complained a good deal of abdominal pain and had to be given enemata several times. In the light of subsequent events it is probable that the urine came away with the bowel movements only. In any case, on December 21st she complained of acute abdominal pain, inability to void, and a distended abdomen. Catheterization yielded 500 c.c. of urine. From that day on she had to be catheterized once or twice daily with a production of anywhere from

200-1,000 c.c. of urine each time. This fact, combined with the patient's depressed state, gave the clinicians great cause for worry, so that every effort was made to search out the basic condition.

Members of the gynaecological, the genito-urinary, the pathological, the radiographic, the neurological, and the surgical services were successively and repeatedly called in, in the course of the next three months, to amend or account for this retention without success, and another major and several minor operations were performed. In view of the fact that the original gynaecological condition had been cured and that no organic lesion sufficient to account for the retention could be found, the decision that the condition was functional was ultimately arrived at, and on March 29th the patient was sent home in the hope that the change would result in improvement of the urinary retention and the constipation.

After several weeks more of daily catheterization and enematization in the outpatient department, she was referred to the neurological clinic. On her first visit there a thorough neurological examination was made which disclosed nothing organic, and psychoanalysis was, therefore, decided upon. She received a few "treatments," but a busy outdoor and a difference of language are not very conducive to good results in psychoanalysis. She was, therefore, readmitted to the ward under the neurological service, and strict instructions, in the patient's hearing, were given to the interne in charge that under no circumstances, even at the risk of death, was the patient to be catheterized. In the meantime in fear of the possible consequences, the author kept in constant touch with the interne, and paid frequent visits to the patient to encourage her and to continue the psychoanalysis. She was admitted on May 14th and on May 15th not having voided yet, she was given a turpentine quinine enema, which was effectual and enabled her to void also. She had been greatly distended, and had suffered much pain in the two days preceding this enema, yet she had not voluntarily voided. However, she was shown that she could do so by the help of the enema, but without catheterization. She was then given a daily enema which was efficient both ways, but she was becoming more and more depressed, and on May 17th threatened to commit suicide, so that a day and night guard had to be put over her. This condition continued until the 20th, when believing that she was "just talking" when she threatened suicide, I promised her that if she would once void voluntarily—without

the stimulus of an enema—I would dismiss the guard whom she greatly resented. She agreed and the contract being happily consummated, she was induced to void again the next day. On the 22nd, after voiding again, she was discharged to return to our outdoor clinic. She presented herself there three times in the next three weeks, on the first two of which occasions she stated that she had not voided for the preceding twenty-four hours, and this was confirmed by percussion of the bulging abdomen. However, she was easily induced, on each occasion to retire to the lavatory and return shortly, with the prominence gone. She made one more visit proudly escorted by the outdoor nurse who had been doing the catheterizing about six weeks later, reporting that she had been able to void once, but once only, every day, and that she had had little difficulty with her bowel movements since. In the course of the next year she appeared a few more times to report herself as being well.

Comment

Here, we had to deal with an undernourished, depressed, pallid and unattractive girl of somewhat poor mentality, suffering from hysterical retention. The question was to find the symbolism as manifested in her symptoms and elicited from her "associations," and in the light of these symbols and their interpretation penetrate to and solve the complexes which underlay them. To state that one cannot use stock interpretations of symbols, as one looks up words in a dictionary, and that the interpretation of symbols or the means to do it must come from the patient—through the associations—and not from the psychoanalyst, is to state a truism. However, here we had to deal with a patient who was somewhat difficult of access, possessing somewhat inferior intelligence, speaking a different language, all of which added to the difficulty of working in an outpatient clinic. It was, therefore, decided that a rapid means of approach might be tried, by making use of the obvious interpretation of the motivation determining her symbols (or symptoms) and judging by the results the decision seemed a happy one.

The girl in the last analysis was unattractive in appearance and in manner, she was twenty-five years old, and her hymen was intact. Her emotions were normal, but she lacked the normal appeasement. We knew long before psychoanalysis was established that hysterical women, sometimes by their own confession, liked the

stimulus of a full bladder or rectum to their sexual organs, we knew also that for similar reasons some of these neurotics are rather keen on vaginal or urethral instrumentation. Finally, this girl first came to the hospital, already stating that usually she urinated only once or twice a day, which is by no means the normal number of times. The stage here, therefore, seemed to be already set for a preconceived idea, and instead of the usual method of slow eliciting, I proceeded more on the basis of suggestion, suggestion, however, which was to a considerable extent justified by the associations elicited from the patient. Proceeding, therefore, on this basis, I was able, step by step, to obtain admissions always reluctant, sometimes resentful, which seemed to justify my conclusions more and more. Finally, I judged that by a *tour de force*, which I could carry out only in the hospital, accompanied with further analysis and obviously friendly suggestion I might achieve my aim, with the results as already indicated above.

Conclusions.—This case is instructive from two points of view: (1) The difficulty of most medical men in appreciating a purely psychic element with or without associated organic disease; and (2) the extreme importance for the psychoanalyst of being absolutely certain that he is not treating a purely organic condition.

PHRENICOTOMY IN TRAUMATIC INJURY TO THE CHEST

By W. P. WARNER, M.B.

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We have been unable to find in literature any reference to the use of phrenicotomy in chest injury due to trauma.

Stuertz in 1911 proposed paralyzing the diaphragm on one side so as to rest and relax the lung for the treatment of pulmonary tuberculosis and bronchiectasis. This is done by interrupting the phrenic nerve in the neck (phrenicotomy). Sauerbruch in 1913 reported cases in which this operation had been done with great benefit in pulmonary tuberculosis.

Alexander, in his book *The Surgery of Pulmonary Tuberculosis*, deals at length with the question of phrenicotomy in reference to pulmonary tuberculosis. The details of the operation are not given in the present case report,

but an excellent account of the various operative procedures are given by Alexander. Phrenicotomy is a simple operation done usually under local anaesthesia. The phrenic nerve is exposed in the neck where it runs down on the scalene muscles above the omohyoid just at the outer edge of the sterno-mastoid muscle at the junction of its lower and middle third. The nerve identified, it can be treated in various ways including simple crushing with forceps, (simple phrenicotomy) or by exeresis (radical phrenicotomy).

The results of interrupting the phrenic nerve in the neck are as follows: The diaphragm on that side immediately ceases to contract, and shows only slight paradoxical movements of about one centimeter due to varying intra-thoracic pressure. The paralysis lasts about three months with simple phrenicotomy, with the radical operation it is permanent. Another result of interrupting the phrenic nerve is that after the simple operation the paralyzed diaphragm is elevated into the thoracic cavity a distance of from two to four centimeters. This elevation may be much more pronounced particularly after the radical phrenicotomy. This paralysis and elevation of the diaphragm causes a reduction in the lung volume of from one quarter to one third. The relaxation of the lung and reduction of its volume induces pulmonary rest. The most important factor in putting the lung at rest after phrenicotomy is, however, the elimination of the pumping action of the diaphragm. Therefore in phrenicotomy we have a very simple operative procedure which distinctly puts the lung at rest particularly at its base. The paralyzed diaphragm is lifted and no longer exerts its pumping action on the lung.

Patient, Mr. P. B. age thirty years, was struck on the left side at the costal margin, by an automobile at 5:30 p.m., December 8, 1925. He had been knocked down, and was brought immediately to the clinic, complaining of pain in the left knee and left upper abdomen. He was quite rational, pale, perspiring and vomited several times. On examination the left side of the abdomen was rigid, particularly the upper half, with pain on pressure over this region and localized tenderness over the ninth rib, no crepitus felt. There was no demonstrable free fluid in the abdomen, no distension, liver dullness pres-

ent. The spleen could not be felt. He was admitted to hospital; temperature 98.3°; pulse 80. Seen at six-thirty p.m. he complained of less pain in the abdomen and examination of it showed slightly less rigidity; chest examination, breath sounds normal throughout; a diaphragm descent of 3 cms. on the left side as compared with 5 cms. on the right. No free fluid was demonstrated in chest. Heart and nervous system were apparently normal. Blood-pressure: 125-80. Urinalysis was negative; W.B.C. 24,000; diagnosis at this time; hæmorrhage into either pleural or abdominal cavities. Patient was kept absolutely at rest and pain relieved with sedatives.

December 9th.—Temperature 101°; pulse 100; respirations 24; W.B.C. 27,000. Rigidity of abdomen less. Patient complains of pain in left upper abdomen aggravated by deep breathing. Chest examination as before.

December 11.—No change in general condition. W.B.C. as before. Chest examination showed on the left side, diminished resonance to angle of scapula with absent breath sounds, decreased vocal fremitus and resonance. Fluoroscopic examination showed dense shadow over diaphragm on the left side. Diagnosis—hæmorrhage into left pleural cavity. Treatment—absolute rest in bed with opiates; calcium lactate, intravenous hypertonic saline.

December 13th.—Patient complained of some severe pain in left costal margin. Temperature dropped to 99°. Pulse rose from 90 to 120. Blood-pressure dropped to 90-60. Patient became pale, perspired and looked very ill from hæmorrhage. He complained of pain in left apex, evidently pleural pain, and coughed up small amounts of blood. Chest examination showed dullness posteriorly practically to the apex of the affected side with bronchial breathing and whispered bronchophony. The area of dullness extending anteriorly to the 7th rib in the anterior axillary line. A confirmatory diagnostic puncture of the chest was done in the 8th interspace of the left side and blood obtained. A bleeding time of 3½ minutes and clotting time (Lee & White) of 8 minutes showed that this continued bleeding was not due to any defect in blood clotting mechanism.

The patient therefore had had three hæmorrhages into the left pleural cavity while at rest, despite the use of therapy intended to decrease

his blood clotting time. The presence of apical pain and pain at the left base on deep breathing along with the coughing of blood, showed that the hæmorrhage was coming from torn lung and probably torn diaphragm. The third hæmorrhage was so severe that the patient was in no condition for an open operation into the thorax, with rib resection, cleaning out of blood and local hæmostasis.

It was considered that the next thing to do would be to put the diaphragm at rest, thereby stopping any hæmorrhage which might be coming from it. Also it was thought that if the lung could be put at rest, elevated in the thorax and saved from the pumping action of a contracting diaphragm any hæmorrhage coming from it would stop. Whatever was undertaken in an operative way had to be done with very little shock to the patient. Simple phrenicotomy was suggested by Dr. Colbeck as being the proper procedure at this stage, and he performed the operation on the left phrenic nerve under local anaesthesia with no discomfort or shock to the patient. The diaphragm and lung were thus put at rest with no operative shock and the hæmorrhage controlled. Fluoroscopic examination after phrenicotomy showed the left diaphragm to be about 3 cms. higher than before operation. There were only slight paradoxical movements present.

The paralysis is temporary and the muscle will begin to contract in about three months. The subsequent course of the patient's illness showed nothing remarkable. He had no further hæmorrhages and temperature and leucocyte count shortly returned to normal. The pain in the left chest disappeared and he has practically regained his former health.

NON-TOXIC GOITRE WITH NERVOUS SYMPTOMS

By H. O. FOUCAR, M.D.

London, Ont.

A professional man, aged forty, who has had a goitre since boyhood, was well until two years ago, when he noticed that he was becoming nervous and irritable and that his heart action was rapid and irregular. These symptoms seemed to follow a psychic shock. On examination he appeared to

be a man under nervous tension, and from the history, we would not have been surprised to find the classical signs of hyperthyroidism. These, however, were absent. None of the eye signs were present, the skin was normal, there was no tremor of the fingers. He was gaining weight. His thyroid was definitely enlarged, soft and apparently of the colloid type. No thrills or bruit were demonstrable over it. His heart action was increased (80-96 beats per minute) and irregular, due to numerous extrasystoles. No cardiac enlargement was present. His systolic blood pressure was 95 and the diastolic 70. This patient was seen with a view to the advisability of surgical intervention. It was felt, however, that his colloid goitre was purely an incidental finding, and was not responsible for his nervousness, tachycardia or palpitation. These symptoms were probably the result of chronic nervous exhaustion in a hypertonic type of individual and treatment was outlined on that basis.

Patients in this group present a definite diagnostic problem. Casually viewed, they are likely to be regarded as cases of hyper-functionating goitre and very often surgical treatment is advised. It is quite possible to have these goitres removed, but it is of prime importance to differentiate between a simple non-toxic goitre with general nervous symptoms due to acute or chronic nervous exhaustion, and a true toxic goitre, with nervous and general symptoms as a

direct result of the disturbed function of the thyroid. Needless to say, the management of each type is entirely different. *Bulletin of The Harvey Club, London, Ont.*

PITUITARY EXTRACT IN ASPHYXIA PALLIDA

By J. B. MANN

Peterborough

Baby R., son of a para-two mother, showed signs of partial asphyxia after a ten-hour normal labour. Very little difficulty was experienced in starting respiration, but in spite of ordinary methods of stimulation, the breathing was shallow, although the accessory muscles were used. The skin was pale and cold. The baby made no voluntary movements. Application of hot blankets and hot water bottles for two hours failed to warm the body surface or bring any change in colour. Finally, two minims of pituitary extract were injected intramuscularly. In fifteen minutes, the skin began to become pink and in about five minutes more, he began kicking vigorously and behaved otherwise as a normal infant. The change was very dramatic. Further progress was uneventful. *Minutes of The Harvey Club, London, Ont.*

Anaemia in Hypothyroidism.—Three cases of anaemia in hypothyroidism are reported by George M. Mackenzie, New York. It is of interest that in all three of these patients a diagnosis of pernicious anaemia had been made prior to determination of the basal metabolic rate. Only one of the three patients had a gastric analysis, and this examination showed an absence of free hydrochloric acid. In two of the patients, urobilin excretion was determined and showed no increase. That the anaemia of these patients was not merely a concomitant of the hypothyroidism and due to some other unrecognized cause is a conclusion justified by the effects of thyroid therapy, which was the only form of treatment employed. No iron, arsenic or transfusions were given. Mackenzie states that, for differential diagnosis, the symptoms of sensitiveness to cold, diminished perspiration, a yellow

tinge of the skin about the eyes and malar regions are important. Determination of the basal metabolic rate and the urobilin excretion supply, however, the most essential data for a diagnosis. Mackenzie's patients manifested no or very slight characteristics of myxedema, such as increase in weight, puffiness of the face and thickening of the skin, mental impairment, alteration in quality and quantity of hair and constipation. The most conspicuous symptom was weakness; sensitiveness to cold, decreased perspiration, paresthesia of the extremities, palpitation and dyspnea on slight exertion were also noted. The blood picture suggested primary anaemia, but alteration in the size and form of the red cells was slight or entirely lacking. The basal metabolic rate before treatment was between —18 and —44.—*Jour. Am. Med. Ass.*, Feb. 13, 1926.

Retrospect

RECENT ADVANCES IN HÆMATOLOGY

II.—LABORATORY AIDS IN THE DIAGNOSIS OF ANÆMIA

BY EDWARD S. MILLS, B. Sc., M. D.

Montreal

The modern tendency in clinical medicine to seek the aid of laboratory methods in the diagnosis and prognosis of disease has resulted in the evolution of scores of special tests. These, like clinical signs or symptoms are in no sense diagnostic of any one disease entity because they are merely indices of certain physiological or pathological processes. For instance, a direct positive van den Bergh is no more diagnostic of obstruction in the common bile duct than blowing breathing is of pneumonia. The successful use of these laboratory aids, therefore, depends upon a knowledge of the factors upon which they are based. In no instances is this more true than in the differential diagnosis of anæmia. Consequently, it is intended to briefly mention the more common tests now in vogue and to limit the discussion largely to their interpretation.

(A) TESTS TO SHOW

INCREASED BLOOD DESTRUCTION

Such tests depend upon the overproduction of bilirubin and urobilin, pigments which normally result from the physiological wastage of red blood cells¹. When these undergo destruction in the spleen, and probably elsewhere in the reticulo-endothelial system their hæmoglobin is changed to bilirubin. Just how this takes place is not known but it has been recently shown that blood of the splenic vein contains more bilirubin than that of the splenic artery². This pigment circulating in the blood probably in combination with protein, is set free and excreted by the liver. In the intestinal tract by the action of bacteria a part is changed to urobilinogen which is reabsorbed into the portal circulation from which it is again removed by the liver, reconverted into bilirubin and excreted in the bile as such. In any condition, therefore, where

there is abnormal red cell destruction, (and bilirubin formation) this will be reflected in the bilirubin excretion and urobilinogen production provided liver function is not greatly impaired and there is no biliary obstruction. If the rate of urobilinogen formation exceeds that at which it can be removed from the portal stream by the liver it will enter the general circulation and be excreted in the urine. It is therefore clear that excessive urobilinuria and increase in plasma bilirubin may result from two entirely different pathological processes namely, hepatic insufficiency or some hæmolytic process whether it be for instance, Addison's anæmia or hæmolytic jaundice. On the other hand when there is complete obstruction to the excretion of bilirubin by the biliary tract as in obstruction to the hepatic or common ducts by stones, this substance will not reach the intestine and no urobilinogen will be formed. Examination of the urine would reveal bilirubin but no urobilin³. This then is the basis for the following tests.

(a) *Van den Bergh test for bilirubin*⁴.—To blood plasma are added reagents consisting of sodium nitrite and sulphanilic acid. If directly positive a purple colour appears. If this is negative the proteins from the plasma are precipitated by alcohol. The test is repeated. If a purple colour now appears it is indirect positive. For this difference the following explanation has been offered. Bilirubin arising from the destruction of red corpuscles exists in combination with protein. When it reaches the liver it is freed from the protein and excreted in that state. If, however, there is biliary obstruction the freed product will be thrown back into the circulation. Instead of an indirect, a direct reaction is now obtained⁵. Caution must however be exercised in using this alone as a measure of differentiating obstructive from hæmolytic jaundice. Although originally devised as such, it has been the author's experience that it is not always reliable. For instance, if one makes repeated van den Bergh's tests on catarrhal jaundice cases, one occasionally obtains graduations of the reaction at one time or another during the course of the disease. Then again, a recent case of undoubted hæmolytic

jaundice gave a direct test which could not be interpreted as biliary obstruction.

(b) *Icterus index test for bilirubin*.—This is a roughly quantitative test for plasma bilirubin devised by Meulengracht (1921)⁶. Plasma matching the standard solution, which consists of potassium dichromate and sulphuric acid in aqueous solution, has an index of 1. If the plasma is diluted four times before it matches the standard, the index is four. Normal plasma has an index of 4.4. In hæmolytic diseases the index may rise to nine or twelve; in obstructive jaundice from forty to ninety, as recently shown by the modified method of St. George and Brown (1925)⁷. The test is, however, as the name implies, merely a means for the estimation of pigment in the blood plasma and is therefore in no way diagnostic of any one type of anæmia.

(c) *Fluoroscopic methods for urobilin in urine*.—These were unreliable until McMaster and Elman (1924)⁸ devised a method of maintaining the zinc acetate alcoholic diluting fluid (which with urine containing urobilin gives a fluorescence) at a fairly constant concentration. Dilution with this fluid is continued until the fluorescence can no longer be detected.

(d) *Ehrlich's aldehyde test for urobilinogen in urine*.⁹—This test depends upon the formation of a pink colour on the addition of the aldehyde reagent to the urine. Specimens rich in urobilinogen will give the colour in high dilutions. Normally the dilutions obtained range between 1 to 5 and 1 to 20; in cardiac decompensation from 1/30 to 1/100; and in cirrhosis of the liver and pernicious anæmia from 1/50 to 1/500 or even higher. These figures are however only relative. In fact neither of these tests for urobilin are truly quantitative but they seem to be sufficiently accurate for clinical purposes. Within the last two months Lichenstein and Terwen¹⁰ have claimed a more accurate method.

(B) MEASUREMENT OF RED BLOOD CELLS

It has long been recognized that in pernicious anæmia there is a tendency for the production of abnormally large red cells and that when a large number of all types are measured, the average size is above normal. Many have claimed that this is even more characteristic of pernicious anæmia than a high colour index. On the other hand the size may be almost normal

as in chlorosis while the hæmoglobin is low, or both may be well below the normal as in many of the secondary anæmias. In speaking of size either cell volume or cell diameter may be adopted though it is important to bear in mind which one is being utilized. The methods by which these determinations are obtained are, in the main, easily carried out.

1. Measurement of volume of average red cell.

—A sample of blood is obtained by venipuncture and kept fluid by a pinch of potassium oxalate. The number of cells per c.mm. of blood are counted by means of a hæmocytometer in the usual way. The total cell volume is obtained by centrifuging a specimen of blood at a high rate of speed until the cells are packed down to a constant level. The percentage volume of cells (plasma to cells) can now be directly measured and the volume for any given amount of blood calculated.

$$\text{Volume of average cell} = \frac{\text{Total volume of cells in any unit volume of blood}}{\text{Number of cells in same volume of blood.}}$$

Normally this works out to 8.8×10^{-11} c.cm. while in pernicious anæmia it may be 12 or 13×10^{-11} c.cm. In other types of anæmia it may drop to 5 or 6×10^{-11} c.cm.¹¹.

2 Measurement of diameter of average red cell.

—This may be done in two ways. Price-Jones¹² first applied this direct method of measurement to anæmia. He measured the images of 500 cells as they appeared upon a ground glass screen from a dry smear magnified and projected by a microscope. This method has been recently modified by Grosh and Stipel¹³ who utilized a micrometer ocular to read off the size directly.

The second method is by means of an optical instrument¹⁴. This consists of a system of lenses for throwing a parallel beam of light upon a ground glass screen. If a dried unstained smear of blood is held up to a light a series of coloured rings or coronas (the spectrum) are produced. Their diameter varies inversely as the diameter of the average red cell. By interposing a dried smear into this beam of light the size of the corona (the second red is used) can be measured on the screen, and the diameter of the average cell readily computed. A pocket instrument, calibrated to read off the diameter of the cell directly in mm. has recently been devised by

Dr. F. Emmons of Montreal. The disadvantage of this instrument is that it gives not the average diameter of red cells but only the diameter of the prevailing type of cell.

(C) SUPRAVITAL STAINING METHODS

These methods have come into general use largely through the work of Florence Sabin and her school. There are many dyes in use. Among these are vital neutral red, janus green, and brilliant cresyl blue. The dyes either in aqueous, or alcoholic solution are allowed to dry on a slide. A drop of blood on a cover slip is brought to touch the stained slide. The blood spreads out by capillary action in a thin film between the slide and the cover slip. The edges are vaseline. The dye dissolves in the plasma and is taken up by the cells. For the erythrocyte the common stock solution is aqueous brilliant cresyl blue¹⁵. This stains the leucocytes, the platelets and the reticulum of immature red cells. From such smears the number of platelets and the percentage of reticulated erythrocytes may be crudely estimated.

Discussion.—These are some of the more common special tests used in differentiating the various forms of anæmia from each other and from other diseases. That not one alone is pathognomonic of any one disease entity must be admitted.

(a) Red cell destruction

Normally $\frac{\text{Red cell destruction}}{\text{Red cell production}} = \text{unity}$.

(b) Red cell production

Anæmia or plethora results from a disturbance of this ratio. Either may be brought about by alteration of (a), of (b) or of both. There is no one laboratory test for either. From the estimation of urobilin and bilirubin the amount of red cell destruction may be roughly gauged.

From the estimation of the size of the red

blood cell and the percentage of immature ones in the circulation, their rate of production may be guessed.

In aplastic anæmia red cell production is as a rule alone concerned and this is also true of many of the secondary types of anæmia such as in hæmorrhage or cancer. In these instances tests for urobilin and bilirubin should not show increased amounts of these pigments so long as liver function remains relatively normal.

In pernicious anæmia, however, there is not only increased blood destruction but abnormal blood formation. In addition to the evidences of marked destruction numbers of immature blood cells such as megalocytes, normoblasts, megaloblasts, and reticulated reds make their appearance in the circulating blood.

In interpreting these various laboratory tests, therefore, the clinician should bear in mind the principles upon which they are based and consider them only as an adjunct to the information he has already obtained at the bedside.

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The Pes Cavus of Congenital Syphilis.—The cases observed by C. W. Goff, South Manchester, Conn., in which a positive diagnosis of congenital syphilis was made, showed many characteristic stigmas. A pes cavus, generally bilateral, occurred in practically every case of congenital syphilis and did not occur in the control cases that were free from syphilis. This pes cavus with its characteristic pseudo-hammer toes, Goff avers, constitutes a new, hitherto undescribed stigma of congenital

syphilis, and apparently is dependent on a neuromuscular condition for its pathogenesis. This is denoted further by a very slight scoliosis, tilting of the pelvis, muscular tautness of the hamstrings and variability of the reflexes. Posture and wearing of high heels have no influence in the production of the pes cavus of congenital syphilis. This type of pes cavus is not progressive and rarely gives rise to symptoms. Anti-syphilitic treatment seems to diminish this deformity.—*Jour. Am. Med. Ass.*, Feb. 6, 1926.

Editorial

COMPLEMENT IN HEALTH AND DISEASE

IN ordinary everyday language we speak of the complement of anything as that which completes it. This is a simple definition which, though it may not always be realized, is exactly descriptive in immunology of certain substances in the blood serum which do serve to complete certain processes in the maintenance of health. Elementary as this may appear to some, there are probably a good many practitioners who put aside all consideration of immunological reactions, because of the apparent obscurity of many (and real obscurity of some) of the terms used in connection with them: but who would gladly be given a clear view of the subject. To such we would recommend Professor Cadham's paper on "Complement in Health and Disease," which appears in the present issue. His work has been directed towards the solv-

ing of problems which have heretofore been hardly approached. He has determined the degree of complement present in a series of healthy subjects, and has compared his findings with the quantities found in a series of people suffering from various diseases. While it may be at the present difficult to estimate exactly the value of these findings, they must be regarded as extremely suggestive in their bearing on prognosis and treatment. The absence or lowering in amount of the complement and in some cases its absence appears to be of grave prognostic significance justifying attempts to stimulate its production. Professor Cadman raises points of absorbing interest, and this in itself is of value: but in addition, he has contributed original research which may prove of great value in the practice of medicine.

ON EXTRA PLEURAL THORACOPLASTY

IF to a physician of a generation ago, or less, supposing he were a sort of Rip Van Winkle, M.D., suddenly reappearing in a modern operating theatre, it were intimated by a young surgical confrère that the operation about to be performed was the removal of considerable portions of eleven ribs on one side for the relief of advanced chronic pulmonary tuberculosis, can one imagine his feelings of horror, indignation, even condemnation? There is, indeed, still abroad too much of the *omne ignotum pro magifico* spirit even in circles of the elevated eyebrow, much less worthy of "science" than the decent, if unreasoning, empiricism of the humble practitioner of pre-laboratory days. But that is the counterfoil, for contrast's sake, to the opposite reflexion, that progress is apt to suffer from the ignorant opposition

of the school whose congenital or acquired attitude of mind is *omne ignotum pro detestabile*. Too much action, too much reaction! Both, doubtless, are necessary, indeed inevitable. And a true balance is struck only when there are weights on either side and when the weights neutralize each other.

So with the question of the surgical treatment of pulmonary tuberculosis! Through much ill-advised, uncritical enthusiasm, through much ignorant, and equally uncritical obstruction, operation, even bloody operation, has won its assured place as a valuable arm in the general battle with tuberculosis.

These reflexions have been suggested by a reading of several books and numerous articles dealing with this particular subject that have been recently pub-

lished. Alexander's¹ book, of 350 pages, the first comprehensive review written in English; Gravesen's² book, of 155 pages, incorporating the large experience of Saugman and his successor, the author, at Vejlefjord Sanatorium, in Denmark, also written in English, though with the help of "Dr. Mary P. Nannetti from Scotland"; Brunner's³ book of 375 closely printed pages, a monograph from the Munich Clinic of Sauerbruch, which appeared in 1924; and Sauerbruch's own long chapter in his monumental work on Thoracic Surgery of 1922—all testify to the growing importance of this new field of surgery. In the bibliography of Alexander's work, one counts 500 references. The *Canadian Medical Association Journal*⁴ has already published an article and an editorial concerning this subject.

Extrapleural thoracoplasty, which means the removal of portions of the first to the eleventh ribs inclusive, is now generally accepted as a standard operation. While the technical difficulties are not great, it is no operation to be done indiscriminately by the average surgeon. As pointed out recently with much emphasis, the proper selection of patients is the most important part of the problem. Only the chronic, chiefly unilateral, cases should be considered. Operation during activity can only do harm. Some evidence of resistance in the form of scar contraction of the lung should be demanded. If the trachea, or the mediastinum and heart, are not deviated towards the side affected by the pull of fibrotic lung, operation is not ordinarily to be considered.

As to the operative procedure itself, growing experience is strongly in favour of two-stages as opposed to the earlier one-stage; and also in favour of a general anaesthetic with nitrous oxide or ethylene helped out by a strictly moderate amount of novocain, as opposed to a local anaesthetic alone.

The results are now surprisingly good, and the mortality ascribable to the operation surprisingly low, and these facts deserve to be more widely known. One finds still current the impression that the operation is not only formidable but also

mutilating, deforming, crippling. Two paragraphs from the first chapter of Alexander's book merit quotation.

"At the present time only relatively few cases of far advanced tuberculosis are receiving the benefits of surgery. The majority of these cases have pulmonary cavities, and had been treated without success for months or years with modern sanatorium methods, including artificial pneumothorax. Almost without exception every patient operated upon would have died of tuberculosis if operation had not been performed.

"Thirty-seven per cent of the surgically treated cases in all countries in recent years have actually been cured and another twenty-four per cent decidedly improved. Five per cent were unimproved or became worse; the immediate or direct operative mortality was approximately 1.5 per cent and the additional mortality during the first six weeks from causes indirectly connected with operation, only twelve per cent. The remaining nineteen per cent include the deaths that had no connection with operation; most of them were caused by progression of the tuberculous disease in the unoperated lung or other causes."

These figures are based upon a review of over 1,100 reported cases. In Canada, the latest report covers sixty-five cases of extrapleural thoracoplasty, exclusive of tuberculous pyopneumothorax. Of these, none died from operative shock; four died as a direct consequence of the operation from the eighth day on to the end of the second month, that is about six per cent; *thirty-four per cent were "practical cures," living, working, without cough or positive sputum, reckoned only after the lapse of one to eight years subsequent to operation*; and approximately twenty-nine per cent died from the progress of the disease, usually, indeed, from a relapse following a temporary improvement due to the operation. Of the balance, a considerable proportion were greatly improved; a smaller number moderately improved, or unchanged. It appears that one can count in properly selected cases upon seventy per cent of encouraging results, while in thirty per

cent the operation fails to stay the natural course of the disease, and in six to twelve per cent actually hastens death. These remarks apply to the standard operation, which is applicable to the great majority of the candidates. It fulfills the accepted requirements of the general treatment of the tuberculous lung—rest primarily, and compression if possible. But there have arisen many other operations, variants of the standard thoracoplasty, or new methods for particular circumstances. Thus, Alexander warmly recommends a change in the usual order of rib removal as recommended by Sauerbruch, which is, lower ribs first and upper ribs two weeks or so later, on the ground that pneumonia is a grave danger because of interference with cough after the first stage. He says one should remove the upper ribs first, and the lower ribs last, expecting, thereby, to reduce the operative mortality from that cause. This is a matter of fundamental importance, but has yet to be tried out. The newer work also devotes considerable attention to Jacobæus's method of cauterizing, through a thorascop, single or several adhesions in the shape of bands,

which may be restraining the otherwise good effect of an artificial pneumothorax. Recent literature, particularly Gekler's⁵ article, reports the opening and antiseptic treatment of tuberculous cavities in the lung, with results that are moderately encouraging. The argument as to the relative advantages of operation and artificial pneumothorax goes on, and the tide seems to be turning, at any rate in debatable cases, in favour of thoracoplasty. Space fails us to refer to many other aspects of this question, which is becoming almost daily of greater importance to the large army of the tuberculous, and to those who care for them. It is safe to say that surgery has put forward nothing for many years past of greater credit to its science—nothing certainly which brings a brighter ray of hope to so many otherwise hopeless sufferers. E. ARCHIBALD

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ON THE STANDARDIZATION OF IMPORTANT DRUGS

ATTENTION is directed to the article in the present issue in which a report is presented by Dr. Ward of the Dominion Research Laboratories, on the great variation in strength of the preparation of two important articles in the pharmacopœia, as presented for sale in the various pharmacies of the Dominion. No drug in our pharmacopœia is more important than digitalis, and it is a matter of consequence that every physician in prescribing this drug should know exactly the strength of the preparation with which he deals. Thus far only two out of our many drugs have been examined, but we trust that when the result of this limited examination is presented to the profession an emphatic demand will be made that all important drugs be standardized by the govern-

ment. The necessity for this standardization is being recognized in every civilized country. In the United States, standardization was demanded for many drugs in their pharmacopœia of 1914. In the one just issued the number for which standardization is demanded is greatly increased. Last year, the Therapeutic Substances Act passed into law in Great Britain, and in a recent article in the *British Medical Journal*, the passing of this law is spoken of as a notable event in the year, and of the greatest importance to the progress of medical science, and to the success of medical practice in many cases of sickness; in the case of not a few drugs, the safety of the public is also involved. The Medical Research Council in Great Britain for many years has appealed to the government for

accurate standardization of therapeutic substances to be carried out by biological measures, and in 1916 referred to the absence of this control and standardization as discreditable to the national position of Great Britain in the world of science, and a source of grave danger to the community.

For many years resolutions demanding such standardization for drugs have been passed at every annual meeting of our Association. It is with much pleasure, therefore, that we note that the work of standardization is definitely begun, and we are very hopeful that it will be carried on until all our more important drugs are obtainable in standardized preparations.

Under the auspices of the Health Committee of the League of Nations, two international conferences have been recently held to discuss the possibility of providing stable standards of reference and agreed methods of biological assay for the following medical substances: pituitary extract, insulin, digitalis and other heart tonics, thyroid gland preparations, salvarsan and its analogues, male fern and other an-

thelmintics, suprarenal preparations, ergot and all preparations used for their vitamin content. At the last congress definite agreement was reached in regard to the first seven of the drugs above mentioned, and provision was made for the preparation and preservation in state institutions of international standards of reference. Great Britain has assumed the responsibility for insulin. A supply of insulin was converted into the form of the dry, stable hydrochloride. After repeated purification this hydrochloride was forwarded to the insulin committee of the University of Toronto for an exact determination of its activity. Simultaneous determinations were made by other laboratories in the United States and Great Britain. The results from these various institutions varied only slightly, and the International Conference has accepted the recommendation of the Toronto committee that this preparation should be preserved at the National Institute in London, and become the international standard of strength; one milligramme of which should contain exactly eight units.

VITAMINES

AT a meeting in the Section of Comparative Medicine of the Royal Society of Medicine, held at the end of January last, Professor Plimmer read a paper on the effect of a partial deficiency of vitamins in foods. (*Brit. Med. Jour.*, Feb. 6, 1926, p. 239) and Professor Drummond stated that the fat soluble anti-rachitic factor called vitamin D had been synthesized from chemically pure cholesterol, and that we were within measurable distance of isolating it in a chemically pure form. Professor Evans, as the result of work carried on during the past few years has shown that there was also a third fat-soluble factor, vitamin E, which he regarded as necessary for reproduction. In his paper Professor Drummond insisted that vitamins were not mere hypothetical substances, nor even bodies of completely unknown chemical structure,

but were substances concerning whose chemical nature a good deal was already known. He described the fractionizing of cod liver oil, and showed that the whole of the fat-soluble vitamins were contained in the one per cent of non-saponifiable matter in the oil. Half of this active residue was cholesterol, and was inactive. Fractional distillation of the remainder under low pressure showed that the whole of the active portion was contained in the fraction boiling between 180 and 200 degrees Centigrade at one to two millimetres Hg. pressure. This active fraction consisted very largely of an unsaturated alcohol and contained only the elements carbon, hydrogen and oxygen.

Vitamins are found to be substances of extraordinary potency. In the case of this vitamin D the daily dose necessary

for a rat is less than 0.0002 milligrammes. Amounts as small as this resemble the minute amounts in which the internal secretions control the metabolic reactions in the body.

The early experiments on vitamins were qualitative in nature and directed to ascertaining the distribution of these substances in foodstuffs. The tests undertaken to determine their presence were made as short as possible, and when diets were made quite vitamin-free acute diseases developed within a few weeks. These diseases in the severe forms which develop in complete absence of vitamins in the dietary, are rarely met with in this country. Professor Plimmer, however, has recently studied the effect of partial vitamin deficiency, extending his experiments over months instead of weeks, and has found that when vitamins were present in insufficient amount, a series of effects developed which may be considered as among the commonest complaints of civilized man. One of the notable effects arising from a deficient amount of vitamin B in a dietary was an intestinal atony, inducing more or less stasis of the bowel leading not infrequently to an intestinal toxæmia. Professor Plimmer found that in order to maintain animals in full health their diet demanded the presence of a comparatively large amount of vitamin B. The amount of whole wheat bread required to protect a pigeon from signs of deficiency of vitamin B was no less than seventy-five per cent of the total diet. He also found that amounts of this vitamin re-

quired by different animals to supply their needs varied greatly. The rat requires only one-third as much vitamin B as does the fowl. Care must, therefore, be taken in applying results obtained on laboratory animals to man. It is now generally recognized that deficiency in any one of the four vitamins will produce similar effects in man as in animals, but we are not yet able to state the relative quantities of any of these vitamins demanded in man's dietary; we must recognize, however, the possibility of deficiency in any of these vitamins producing definite disease in man.

The subject is of great practical importance. Professor Plimmer's experiments suggest the possibility that a large proportion of the colics and more serious disorders of the alimentary tract in man may be attributed to a deficiency of vitamin B in his diet; a deficiency produced by the small quantity of whole meal bread which enters into the dietary of most of us. If Professor Plimmer's conclusion is borne out by future experiments, it is obvious that every possible endeavour should be made to induce our population to eat more whole meal bread. Unfortunately, this may involve serious consequences. The transport and keeping of whole wheat flour presents certain difficulties, and farmers are dependent on the supply of wheat "offal" for feeding purposes on the farm. It is evident that further researches on these points must be pursued on a large scale and on as great a variety of animals as possible.

FOCAL SEPSIS

DURING the past year a number of papers and discussions dealing with focal sepsis have appeared. In practically every case the term has been used as signifying a more or less invariable quantity, and the great variation in virulence of different foci ignored. The aching tooth with inflammatory changes in the tissues about its roots presents a very different problem from that of the

painless tooth with cavity formation, erosion and absorption, all active at the apex; the latter condition being far more liable to cause systemic symptoms than the former. The virulence of the bacteria, too, must vary in different cases, causing a wide range in the severity of the infection.

It does not follow that removal of a focus, after secondary changes have oc-

curred will suffice to neutralize these changes, and if the general resistance be much lowered it will, almost certainly, not do so. Still, it is poor practice to burden the system with toxins which can be relatively easily removed.

The difficulty of determining, at times, the presence or absence of a focus is well known to all. Some time ago a man came to me with signs of glaucoma in the prodromal stage. Treatment and the removal of some teeth seemed to restore him to normal. A year or so later he wrote from California, that he had had several operations on his nose and that finally a teaspoonful of pus had been found under a tonsil, the presence of which there had been no reason to suspect. Had this man's general condition been poor, it is quite likely that the complete relief from symptoms which he experienced after evacuation of the abscess, would not have occurred.

Recent work seems to raise the question, as to whether we are justified in stating the problem of lowered resistance in the negative terms usually employed, or whether we must use the positive terms of an active toxæmia, which enables infection to be established. The latter view is supported by one or two observations published during the past year.

Experience during the war demonstrated that healthy tissue can to a very considerable extent protect itself against bacterial invasion. This fact was also clearly shown a number of years ago by Dr. Clarence Webster at McGill, in his experiment on dogs. In this work, cultures were injected under the peritoneum of dogs fed on rancid meat. In every case acute peritonitis developed, while in the controls fed on wholesome food, in no case, did peritonitis follow. Gye, in his recent epochal work, has shown, that no growth has been obtained from his cultures except in the presence of some

principle, apparently toxic in nature, derived from the body. Bond has shown, that the normal excursion of leucocytes does not take place from a clot of pneumonic blood, but that when the vitiated serum is removed by washing with saline, the suspended activity of the leucocytes is restored.

In all these instances there is evidence of the presence of a positive toxic principle and the paper by Osgood (*B. M. J.*, February 20, 1926) quotes a number of authorities who consider that rheumatoid arthritis is, in part at least, due to a diathesis, the significance of which is variously interpreted.

It begins to look as though we shall have to study the nature and incidence of toxins more closely, but chimerical though the identification of toxins may at present appear, the recent investigation, showing that vitamine D, closely resembles cholesterol, proves that such work is quite practicable. More knowledge, too, is necessary to determine the respective rôles of serum and of leucocytes in health and disease, as it is being held by some that the latter attack only dead germs. Bond's work also indicates that when pronounced toxæmia is present the leucocytes cannot do even this.

Evidently lowered resistance is in many, if not in all cases, due to the presence of a toxin in the system, and those who claim that infective disease is due to toxæmia, as well as those who say that it is due to the activity of germs, are in a measure right. The old claim, recently advanced again, that as septic foci do not in all cases cause distant symptoms that the latter are never due to focal sepsis, is about as sound as to argue that neither syphilitic nor tuberculous iritis occur, since there are thousands of cases of these diseases in which the eye is not affected.

R. KERRY

HUMAN AND BOVINE TUBERCULOSIS

IN an interesting article in the *Journal of Medical Research* (Park and Krumwiede, *Jour. Med. Res.*, 27, 109), on the relation of bovine to human tuberculosis, it is stated that all pulmonary tuberculosis is due to the human type of the

bacillus, while one tenth of the tuberculosis of bones, joints and lymph nodes in adults and one fourth of this tuberculosis in children is due to the bovine bacillus. The figures of the English Royal Commission on bovine tuberculosis and those of the German Commission were in essential agreement. As a result of their investigation it would appear that from six to ten per cent of the deaths from tuberculosis below the age of five years must be attributed to the action of the bovine type of the bacillus manifesting itself chiefly in miliary tuberculosis and tuberculous meningitis. The two types of bacilli are to a certain extent mutually exclusive. Pulmonary tuberculosis due to the human type, and the so-called surgical tuberculosis due to the bovine type are seldom found together. Bovine tuberculosis would now appear to be endemic in all parts of the world. Its prevalence in certain districts is, however, very variable. The average figure given for the United States is in the neighbourhood of five per cent, but in certain regions it would appear to exceed eighty per cent, and in others, in which tuberculin testing is ordered by local law, its incidence may be placed at one per cent or even lower. Tuberculosis in cattle menaces human beings owing to the possibility of it entering into the milk supply. Meat under ordinary cooked conditions is not dangerous. Tuberculosis in cattle, while usually a chronic disease, is more prone to generalization than in man. In its later stages a cow may be as truly consumptive as man and present symptoms as definitely indicative of the disease; cavitation, muco-purulent sputum, extensive ulceration of the intestine, and myriads of tubercle bacilli in the faeces. From the faeces the udder is readily contaminated. Much of the contamination of milk is of this origin. In addition, however, to this mode of contamination

the cow appears to be peculiarly liable to develop tuberculosis of the mammary gland, much more so than the human mother. There is evidence, also, that tubercle bacilli may reach the milk from a distant focus through the blood stream without involvement of the mammary gland. Accordingly, wherever tuberculosis of cattle is met with in any advanced state, tubercle bacilli will be found in the milk supply, and will undoubtedly be liable to infect children who are the chief users of milk and the most susceptible. Pasteurization, however, if properly done will destroy the bacilli, but human fallibility prevents nation-wide perfection in this procedure. The London *Lancet* commenting on recent studies of the safety of this process states: "If commercial pasteurization is to ensure freedom from bovine tuberculosis infection, the plant must be so designed that the milk passing through the machine is brought up to a temperature of 62.5 Centigrade and maintained thereat for half an hour. Nothing else will serve."

Many public and private agencies in many countries have for years sought to eliminate bovine tuberculosis by condemning and slaughtering infected cattle. This undoubtedly is an effective means of ensuring a milk supply free from tuberculosis, but the price is tremendous. Certain lifelong students of tuberculosis state that the goal aimed at—a race of cattle free from tuberculosis—is impossible to be attained by this means. The fact that thousands of cattle react to tuberculin similar to humans from the presence of an encapsulated focus is used as an argument against the establishment of slaughter as a routine measure following positive tuberculin reaction. The failure of vaccination of cattle as attempted some years ago in the States should not completely destroy our hope in this direction.

THE SEASONAL OCCURRENCE OF INFECTIOUS NERVOUS DISEASES

IN an editorial appearing in the *British Medical Journal*, of February 13, 1926, one is reminded of the uncertainty

of classification that accompanied the earlier incidence of encephalitis lethargica, and particularly the difficulty of allotting

to this disease, an entity separate and distinct from such infections as poliomyelitis, meningitis and the cerebral type of influenza.

While many observers strongly contended that epidemic encephalitis and the superior form of poliomyelitis, polio-encephalitis, were one and the same infective process, there remained but a close observation of the seasonal incidence of these infections to completely dissipate this theory.

Encephalitis, in all its epidemic outbreaks has occurred during the first quarter of the year, while poliomyelitis in epidemic form appears almost always during the late summer or autumn. Cerebro-spinal meningitis on the other hand prefers the winter or early spring as the season best adapted to its epidemic manifestation.

Further evidence, by which the separate entity of these diseases may be established is found in the age incidence, poliomyelitis being essentially a disease of childhood, while encephalitis attacks all ages, with a distinct preference for adult life in its clinical manifestations and in its sequelæ.

Its similarity to epidemic influenza has been always debatable, but when we recall (1) the absence of encephalitic signs or sequelæ in any of the great influenza epidemics of recent years; (2) the absence of transference of the disease from person to person; (3) the complete absence of the usual catarrhal or gastrointestinal symptomology of influenza and (4) the dearth of the well recognized sequelæ of encephalitis, in the wake of any great influenza outbreak, we find little justification for believing them to be the same disease. The fact that all three of these diseases occur in the sporadic

form in which isolated cases spring up without regard to time or place, and so appear to link up one epidemic with another, does not signify similarity of cause or kind. Rather may this feature be regarded as a characteristic of all epidemic diseases of the nervous system.

In the editorial above quoted which is based on the observations of Dr. Chalmers, medical officer of health for the city of Glasgow, it is pointed out that prior to the epidemic of meningitis in 1906, the reported incidence of tuberculous meningitis steadily increased, while tuberculosis generally showed no such increase.

Regarding this reported increase of tuberculous meningitis, Dr. Chalmers suggests that the apparent increase was due to sporadic cases of epidemic meningitis, carelessly observed or at least carelessly reported.

Careful serological and autopsy examinations should go far toward clearing up the uncertainty, but yet it is felt that the sporadic case of purulent type and of undiscovered bacteriology is most likely the occasional case that carries the infection from one epidemic to another. Dr. Chalmers has shown from his observation and records in the Glasgow outbreak of 1923-1924, that the "carrier" method of transference, so well established in cerebro-spinal fever, finds little support in encephalitis. The geographical distribution of the cases, and the absence of case-to-case infection throughout the epidemic offers the severest criticism of this theory.

The writer's plea for better and additional notification of these several infections of the nervous system should be echoed by means of the press in all countries where they are prevalent. F. H. MacKAY

NATURE OF TUMOUR FORMATION

IN an editorial on "The Nature of Tumour Formation," (*The Lancet*, February, 20, 1926, p. 463) quotes the recent statement of Nicholson, of the University of London, that he considers tu-

mours as essentially parts of the tissues of the body showing no fundamental difference functionally or anatomically from normal tissues. The evidence available at the present, he states, cer-

tainly indicates that the environmental change to which the cells are subjected is the major factor in the production of the majority of tumours. Normal cells can undoubtedly be stimulated to tumour formation by suitable experimental procedures. The predisposition of the cells of certain individuals to react more readily than the cells of other individuals to tumour producing factors cannot however be ignored. Complete uniformity in this respect in normal individuals or in the normal cells of such individuals is not to be expected. The question remains however whether the normal variations are of such a degree as to become an effective factor in producing either an immunity or a susceptibility to tumour formation in individuals or groups of individuals. The extensive studies of Maud Slye on the inheritance of spontaneous tumours

in mice show not only that the tendency to tumour formation is inherited but that it follows strict Mendelian laws and can be demonstrated as a recessive character with almost the same certainty as can albinism. This investigator has bred strains of mice showing on the one hand the development of spontaneous tumours in 100 per cent of cases, and on the other hand the absence of such tumours in fifteen generations. She also produces evidence that the site and character of tumours can be influenced in the same manner. In view of such evidence while we admit that the cell environment may probably be the determining factor in tumour production, one must not overlook the influence exerted by an inherited hypersusceptibility in the individual and possibly also in certain organs or part of organs in that individual.

CANCER INQUIRY OF THE LEAGUE OF NATIONS—INCIDENCE OF CANCER IN DIFFERENT COUNTRIES

THE health organization of the League of Nations has recently published two volumes describing the results obtained from the study of special problems in cancer. The origin of the enquiry was the remarkable difference in the mortality rates in certain European countries from cancer of the breast and cancer of the uterus. England, Wales, Holland and Italy were selected for special study. In all three the official mortality rates reach a high standard of accuracy. In two of the countries, England and Wales, and Holland, the death rate from all forms of cancer is very heavy; while in Italy the mortality rate is low; but England and Wales contrasts with both Holland and Italy in its much higher rates of mortality from cancer of the breast and uterus. Holland suffers from a high rate of mortality in cancer of the stomach. Italy has a higher rate of mortality than Holland, from cancer of the uterus, but a much lower rate than England and Wales. The conclusions drawn by the committee from an immense

mass of data are set out under nine heads. Unfortunately no satisfactory explanation of these striking differences has been found. It has been conclusively proved that the variations of marriage rate, the age of marriage, the number of children to a marriage, all of which might be thought at first to explain the above differences, throw little light on it. No differences in the method of certification or tabulation do much towards explaining the facts, and it is provisionally concluded that the more frequent resort to surgical treatment also explains little. The committee is satisfied that child-bearing does not predispose the woman to cancer of either the breast or uterus. The sub-committee went into the question of the different rates of mortality within each country, and concluded that these differences far exceeded anything reasonably assignable to chance. The committee also calls attention to a rough uniformity of increase in the mortality rate for cancer of the breast in England and Wales up to the age of sixty-five, and

notes that in the Netherlands there is hardly any increase with age after the group of sixty to seventy, and very little in Italy. The subcommittee have devoted considerable attention to this phenomenon. In each of the three countries one third at least of women suffering from cancer of the breast die without radical

treatment. The committee desires to point out that the results of the enquiry justify the statement that in each of the three countries a large number of persons die every year who even in the present position of medical knowledge might have lived considerably longer if recourse had been had to surgical treatment.

Editorial Comments

VALUABLE CINCHONA ALKALOIDS

The Institute for Medical Research, Federated Malay States, has issued in a recent Bulletin a statement relative to the value of the several alkaloids of cinchona in the treatment of malaria. An investigation was carried out by Dr. William Fletcher to ascertain the value of 'cinchona febrifuge' in the treatment of malaria as a substitute for quinine. The composition of this febrifuge is at the present not constant. It is the name given to the liquor obtained from the bark after the removal of all quinine in it, and contains the remaining alkaloids and certain amorphous alkaloids which have been classed together under the name of quinoidine. These, however, are distinctly more irritating and toxic than the crystallizable alkaloids. In the investigations carried out this "cinchona febrifuge" proved quite as satisfactory in the treatment of malaria as quinine, but was weaker and double the dosage was required. The important point is cinchona febrifuge can be supplied at a much cheaper rate than quinine, and it is suggested that the Government of the Malay States should purchase the entire amount of this cinchona preparation, have it assayed and standardized, and then put up in tablet form and issued authoritatively. It could thus be used in all instances in which large numbers had to be treated, and if given in the larger dose would prove quite as effective as quinine. The object of this research was to show that it is not necessary to keep quinine at the high price, at which at present it is held. There is no world shortage of quinine; in these other alkaloids the profession has an efficient substitute.

SHANTUNG UNIVERSITY

We desire to acknowledge the receipt of a beautifully illustrated report of the Shantung Christian University, the product of co-operative efforts in China, England, United States and Canada. The university is situated in Tsinan, at the cross roads of the Yellow river, of the Shantung railway and the Tientsin Pukow Railway, three of the greatest trade routes of the far East. During the last year the hospital cared for 1496 in-patients, and the dispensary connected with it treated 30,152 out-patients. Patients travelled long distances in order to receive the medical assistance which their own communities were unable to afford them. The nurses training school and university has grown rapidly since its organization ten years ago. It now consists of 46 nurses in training under the direction of a nursing superintendent, assisted by three foreign associates and eight graduate Chinese nurses. The social science department represents an endeavour to make social science a vital practical subject which can be effectively applied to the needs of present day China.

MEDICAL RECIPROCITY WITH ITALY

We have received from the Department of Health in Ottawa a copy of the agreement signed at Rome, May 21st, 1925, to regulate the professional practice of medical practitioners in the respective territories of Great Britain and Italy. This agreement states that medical practitioners holding diplomas issued by licensing bodies in Great Britain, in the British Colonies, in India, and in the British Possessions and Dominions

generally, between which and Great Britain medical reciprocity exists and who are legally entitled through existing legislation, on the basis of their diplomas and inscription in the medical register of Great Britain, to carry on free professional practice throughout the Empire, can be inscribed on the professional registers of the Kingdom of Italy and pursue their professional practice in Italy and its colonies without undergoing any further examination or obtaining any new qualification in the institutes of the Kingdom of Italy.

A CHEAP STERILIZABLE DIALYZING MEDIUM

We copy from the Vancouver Medical Association bulletin the following description of a new sterilizable dialyzing medium which may prove valuable to some of our readers. It was first employed by Dr. H. W. Hill, director of the Vancouver General Hospital laboratory, and Professor of Bacteriology in the University of British Columbia, and is strongly recommended by him as very serviceable. He writes as follows:

In searching for a sterilizable dialyzing membrane, a suggestion came from the Christmas festivities of 1925, which presented much candy and many candy-boxes enclosed in transparent glistening sheets of "paper." The resemblance of this "paper" to thin sheets of collodion induced me to try its dialyzing powers, which for silver nitrate, sodium chloride (Donna E. Kerr and H. W. Hill, independently), and glucose (Donna E. Kerr), proved perfect. The next step was to test its resistance to sterilization. Fifteen pounds steam pressure for twenty minutes in the ordinary laboratory autoclave left it unchanged in appearance, feel, etc.; and its dialyzing qualities were unaffected (Donna E. Kerr).

The various uses of such a membrane in physics, chemistry, and especially in biology and bacteriology, both scientific and applied, are obvious, and need not be enlarged upon here. With Dupont's Household Cement, probably collodion dissolved in acetone (R. E. Coleman), the sheets may be made up into tubes, into flat, square or round bags, etc., etc. Diaphragms may be cemented across bowls or beakers, or glass tubes, etc. It would appear to make practicable a whole field of bacteriology as yet hardly explored.

The material is said to be named "cellophane," and to be made in France (now made by the Dupont Company of U. S. A.). It sells wholesale at about 25 cents a square yard. So far as we have been able to discover, this substance has not been previously advocated as a sterilizable dialyzing membrane, for the above purpose. *Vancouver Med. Ass. Bull.* Feb., 1926.

We would direct the attention of our readers to the notice issued by the Grafton Publishing

Company, Limited, London, England, who publish the Medical Who's Who. In this Who's Who, every member of the medical profession in Canada whose name appears on the medical register of Great Britain, and who makes the necessary returns, has the privilege of having his name appear. This directory includes the names of every registered physician in the Empire and in the various Dominions who takes the trouble to fulfil these conditions. For many reasons it is desirable that those Canadians who can register, should do so.

We publish in this issue an extract from a letter to Dr. John Stewart of Halifax from Professor Adami of Liverpool regarding Professor Blair Bell's treatment of cancer. To present to our readers another impartial opinion regarding the possibilities of this treatment we abstract the following from the Bulletin of the American Society for the Control of Cancer. Professor Francis Carter Wood, Vice-President of the Society and Director of the Institute of Cancer Research of Columbia University, went abroad and spent some time with Professor Blair Bell in Liverpool and also conferred with scientific investigators on cancer both in London and Paris. The following is a short summary of what he learned, stated in his own language.

The Report

I visited Professor W. Blair Bell in Liverpool and was given every opportunity to study the treatment of patients with the lead preparation which he uses, to see those who had recovered from cancer following such treatment, and to get some idea of the method of preparing the drug. The latter consists of a very fine suspension of pure metallic lead made by a very intricate and delicate process, so complicated that only specially trained chemists can make it. The preparation so produced only keeps for three days; after that period it becomes highly poisonous and cannot be used. It is therefore impossible to give this treatment at present except under the conditions established at Liverpool and with full appreciation on the part of the patient of its highly dangerous nature. A great deal of clinical experience is necessary to avoid serious, if not fatal, poisoning from lead. If small doses are given to avoid this danger no effect is observed on the cancer.

Unfortunately lead seems to be the only metal which is effective. A large amount of experimental work has been done by Professor Blair Bell and his colleagues to see if some less dangerous substance might not be useful, but without result. It was therefore decided to try lead on patients with advanced cancer.

The treatment consists of the injection into the veins of the cancer patient of a small quantity of the lead suspension. This injection is repeated once

a week for six weeks. During this period the patient must be in bed and very carefully observed to see that no evidence of lead poisoning appears, and if such evidence is noted the treatment must be immediately stopped.

Of those who are able to take the full quantity about one-fifth receive very considerable benefit. They are so improved in health and the disease is so completely arrested that it is worth while for them to go through with the necessary course of treatment. In the other four-fifths the treatment seems to have no effect on the tumour growth and in them the disease continues its course.

Whether in the future the percentage of favorable results can be increased cannot be stated at the moment, but every effort is being made by a group of chemists in the University of Liverpool to prepare a less poisonous and more permanent preparation so that ultimately the treatment may be used in institutions where all the necessary analyses and blood examinations can properly be carried out.

We have received a copy from Dr. A. C. Jost, Provincial Health Officer for the Province of Nova Scotia of his annual report for the past

year in which evidences of a material improvement in the general health of the province are presented. The death rate is less than that in the previous decade, being only 12.56 for 100. Of each thousand infants born alive there are fewer deaths within the year by twenty or twenty-five. Whereas some years ago the province lost nearly three of its population per day from tuberculosis, during recent years the loss on an average has been only two a day. It is significant that the counties in which nurses have been for the longest time on duty are those in which most public health work has been done and which show the greatest improvement in vital statistics. This is what was to be expected, and can be regarded as a fulfilment of the prediction made when the public nursing programme was undertaken.

Correspondence

COLLOIDAL LEAD IN THE TREATMENT OF CANCER

*Extracts from a personal letter to
Dr. John Stewart, Halifax*

My Dear Stewart,

..... Now, as to Blair Bell's work. I am absolutely convinced that he is on the right lines. Though, as I said in my B. M. J. letter, we have to recognize that in some cases, especially of intestinal cancer, killing the tumour cells means killing the patient, because, when the cancer cells disappear, there is nothing left but so thin a wall that perforation easily supervenes. But, last July, I was privileged to take part in a review of thirty-one out of a hundred and eighty-seven inoperable cases that had been treated up to date. Some ten others were out of the country or on holidays and could not get up to be reviewed. But there was a group of men and women actively about their daily work and—what is more—of good healthy complexion without a sign of cachexia. It was wonderful, and I suppose a thing that has never before been seen in the world.

There are two difficulties before us. The first is one which I hope we shall get over. These colloidal preparations tend to agglomerate and

precipitate, especially when shaken, so that they must be used within a few hours of preparation. If we cannot get over this difficulty it will mean that they will have to be made in big centres by expert physicists. Still I hope that we shall find a way out of this present dilemma. But, even if this be got over, you will realize that the border-line between killing just the cancer cells and the normal cells, and so the body as a whole, is a very narrow one. And when in addition there is a remarkable variation in the susceptibility of the individual you will see the difficulty of encouraging every one to use the treatment. As it is, up to the present moment, of these inoperable cases only little more than one out of every four survives the treatment despite all our care. Think of the holocaust there would be if every doctor in the country took to injecting the lead, and what discredit would come to the method. We have by hook or crook to keep the treatment in the hands of experts and cannot at the present time render it generally available. And we are faced by the not unnatural accusation that we are purposely keeping our methods secret for the personal benefit of Blair Bell. He has got over this by declining to receive any fees for treatment. The fees are paid into the Committee, which is able to employ any

profits that accrue for the purpose of medical research, giving Blair Bell a stipend as Director. I think we are doing the right thing, but you will see that it is not, and must not be, at present generally available.

I find I have slipped almost insensibly into using the words *we* and *us* as I have been so many years associated with the work as an adviser.

Yours ever,
(Sgd.) J. George Adami

The University of Liverpool.
January 11, 1926.

THE ROYAL SOCIETY OF MEDICINE

I Wimpole Street,
London, W. 1.
March 3, 1926.

Dear Sir,

In the course of a recent conversation with the President of the British Medical Association, who is a Fellow of this Society, I mentioned that the Royal Society of Medicine would be much pleased to extend the hospitality of the Society's house to medical men visiting England from Overseas. Dr. Thomson thereupon suggested that I should communicate with the Secretaries of the Overseas branches of the British Medical Association, and with you.

I am delighted to act upon this suggestion and to say that if any member of your Association calls upon me with a letter of introduction from you, I will give him visitor's privileges according to the rules of this Society.

Such privileges extend for one month and comprise the use of the Society's house with its

various amenities, the right to read in the Library and the right to attend any of the meetings of the Society.

I enclose copy of our Calendar, and am

Yours very faithfully,

(Sgd.) G. A. EDWARDS,
Secretary.

Dr. T. C. Routley,
184 College Street, Toronto.

THE USE OF CHLOROFORM

To the Editor:

In the last issue of the *Journal* (March) on page 320 there is a Report on a Discussion at the Royal Society of Medicine on Anæsthesia in Children. I read that Dr. Harold Singleton said, "to induce anæsthesia with chloroform is dangerous as, indeed, is its use under any circumstances."

I have not seen the Reports of the Royal Society of Medicine, and do not know if any one of those present took exception to this opinion, but with your permission I make a protest against the use of such an extreme statement. As an Edinburgh student I was taught that chloroform is a very safe anæsthetic, and especially so in the case of children. My experience of more than fifty years confirms me in that belief. No anæsthetic is absolutely safe, but if chloroform is given *in the proper way* as taught by Simpson, Syme and Lister,* it cannot reasonably be considered a dangerous drug.

Yours faithfully,

(Sgd.) JOHN STEWART

Halifax, N. S. March 13, 1926.

* Chloroform anæsthesia, *Can. Med. Ass. Jour.*, 1914, iv, 1053.

Industrial Investigations in Workshops and Factories.—The investigation of the effects of short rest pauses introduced into long spells of repetitive work has been continued by the staff of the Industrial Fatigue Research Board. Since the comparison made by Dr. H. M. Vernon and Mr. T. Bedford of the outputs in certain factories over periods respectively before and after the introduction of rest pauses, full facili-

ties have been obtained in four factories for practical trials, with continuous observation of the workers. This part of the investigation has confirmed the previous work in showing that the judicious introduction of rest pauses almost always has a beneficial effect, and that the workers unconsciously respond in such a way that their output is increased notwithstanding the shorter time actually worked.—Report Medical Research Council, *Brit. Med. Jour.*, Jan. 23, 1926.

Men and Books

AN HISTORICAL SKETCH OF THE
MEDICAL PROFESSION OF
TORONTO

By. H. B. ANDERSON, M.D.,

Toronto

After the Peace of Versailles, in 1783, the enforced migration of United Empire Loyalists brought some ten thousand exiles, who had risked and lost all for their attachment to king and country, to seek new homes in the northern wilderness, and this constituted the first considerable settlement of the province of Upper Canada.

The sudden influx of a class cemented by the rigours of war, the harshness of the victors and the hardships of the pioneer; the extent to which they acquired possession of the lands of the province and the control of affairs in general which naturally fell into their hands, were unfortunately, perhaps inevitably, the source of many difficulties and much discussion in later years as the population increased by the immigration of more diverse elements from the mother country.

According to Sabine, their American historian, the Loyalists included a large representation of the official classes and the professions of law and divinity, the latter mostly of the Episcopal church. The remarkable fact that few doctors accompanied these exiles, is accounted for by Sabine on grounds reflecting no discredit upon the medical profession. "The physicians who adhered to the Crown were numerous and the proportion of Whigs was probably less in the profession of medicine than in either that of law or theology. But unlike the latter callings, most of the physicians remained in the country and quietly pursued their business. There seems to have been an understanding that though pulpits should be closed and litigation suspended, the sick should not be deprived of their regular and freely chosen medical attendants; . . . their persons and property were generally respected in the towns and villages, where little or no regard was paid to the bodies and estates of the gentleman of the robe and surplice."

A few medical officers of disbanded Loyalist regiments settled in the Lower Provinces, especially in New Brunswick, but some of these removed

to Upper Canada at a later date. To Canadians the best known of these American colonial regiments was the old "Queen's Rangers" commanded by Colonel John Graves Simcoe during the Revolutionary War. At the close of the war the regiment went out of commission, but on being appointed first governor of Upper Canada, Simcoe received authority from the Crown to organize a military force for service in the province. He named this regiment the "Queen's Rangers" in honour of his old command, and the important service it rendered in the settlement of York and the opening up of Yonge Street, before it was finally disbanded in 1802, is recorded in the early history of the province.

The medical needs of the small settlements gathered at first around the military posts and along the St. Lawrence and the Great Lakes, were supplied by the medical officers of the garrisons. As population increased and settlements spread, the dearth of properly qualified practitioners, especially at a distance from the garrisons, led to the springing up of many quacks and irregulars, who menaced the lives of those by dire necessity obliged to consult them. In 1788 an Act, known as the Quebec Ordinance, was passed by the parliament of Canada, which provided under severe penalty, including fine and imprisonment, that no persons should practice medicine without a license from the governor or commander-in-chief of the province, upon certificate of examination and qualification by a board appointed by them for that purpose. University graduates in medicine and warranted army and navy surgeons were excluded from the necessity of examination. This attempt at control, however, did not have the desired effect, and a further legislative enactment occupied the attention of the first session of the parliament of Upper Canada at Newark (Niagara-on-the-Lake) in 1796. This Act provided for the appointment by the governor of the province of a medical board, to be composed of the surgeon to his Majesty's hospital, with the surgeons of his Majesty's regiment doing duty in the province, and all other authorized surgeons and practitioners, or any two of them, of whom the surgeon to his Majesty's hospital must be one, to examine and approve candidates for license to practice. This Act likewise proved unsatisfactory and was repealed in 1806.

That more effectual control was necessary is evident from an editorial in the *York Gazette*, October 8, 1808: "The opinion we maintain of such a public want, arises from the conviction we feel and the knowledge we possess, that the health, nay, frequently the existence of a fellow creature, is lost, being too often sacrificed to the pretensions or cannibal ignorance of empirics, quacks and imposters." The deplorable state of affairs continued and later engaged the interest and trenchant pen of the redoubtable Bishop Strachan and other public men, and finally resulted in legislation establishing the Medical Board of Upper Canada in 1818.

The creation of the Upper Canada Medical Board was the beginning of effective control of medical practice in the province. The board began its duties January 4, 1819, and continued to hold regular examinations and grant licences until 1839, when an Act of the provincial parliament was passed, constituting "The College of Physicians and Surgeons of Upper Canada" with power to examine and licence and otherwise control medical affairs in the province.

This Act was claimed to infringe the rights of the Royal College of Surgeons and after a heated controversy, it was disallowed by the Imperial parliament. The College of Physicians and Surgeons of Upper Canada held its last meeting in 1841 and control of the examination and licensing of practitioners reverted to the Medical Board of Upper Canada and continued under its control until 1865. In 1841 the board appointed by the governor general, Lord Sydenham, consisted of Christopher Widmer, William C. Gwynne, Robert Hornby, Walter Telfer and Henry Sullivan. This medical board was subjected to many bitter attacks, and much criticism on the part of the profession during the period from 1833 until it finally went out of existence.

In 1865 the parliament of Canada passed "an Act to regulate the qualifications of practitioners of medicine and surgery in Upper Canada" by which was constituted the "General Council of Medical Education and Registration of Upper Canada," and this body began its duties January 1, 1866, and after Confederation, under authority granted in 1869 by *The Ontario Medical Act*, the College of Physicians and Surgeons of Ontario was created.

In order to maintain uniformity of examinations and control, provision was made for the admission not only of regular practitioners but also of eclectic and homeopathic practitioners

who had been in practice before 1850. Each of these was to have a fixed representation on the council as the executive body of the College was called. This was brought about by an agreement between the homeopaths, eclectic and regular practitioners to the repeal of Acts passed in 1859, 1861 and 1866, under which respectively, they had obtained legislation, with authority to examine and grant licence to practice in the province. The representation of the eclectic ceased without special enactment about 1875.

The population of Upper Canada at the time York was chosen as the capital in 1793 was about 12,000, composed almost wholly of United Empire Loyalists, disbanded soldiers, the garrisons and official personnel. During Simcoe's four years as governor, the population increased to about 30,000. The only evidences of a settlement at York at the time of Governor Simcoe's arrival, were the ruins of the old French fort Rouillé, (established in 1749 to protect the southern entrance to the overland trade route between Lake Ontario and the Georgian Bay), and a few wigwams of wandering Mississauga Indians.

Dr. James MacAulay, the progenitor of some of the most prominent families in the later history of the province, was induced to come to Upper Canada by his friend, Colonel Simcoe, as physician to his household. Arriving in 1792 he was appointed surgeon to the "Queen's Rangers" and after the regiment was disbanded, he was made Deputy Inspector-General of hospitals of the province. His own name, that of his wife, and other members of his family are commemorated in the streets (Teraulay, Hayter, James, Buchanan, Alice, Edward, Elizabeth) of the district early known as MacAulay Village—later St. John's Ward. On the establishment of the Upper Canada Medical Board, he was elected chairman and continued to act in this capacity until his death in 1822. The name "Teraulay" was derived from the last syllables of Hayter (Mrs. MacAulay's maiden name) and MacAulay.

Dr. John Gamble, an Irishman, born 1755, graduated at Edinburgh and came to New York in 1779, as Dr. MacAulay's assistant surgeon. For a time he was attached to the old "Queen's Rangers" during the Revolutionary War, at the close of which he went to St. John, New Brunswick, where he practised for ten years. In 1793 Governor Simcoe appointed him assistant surgeon to the new "Queen's Rangers". When the regiment was disbanded he removed to Kingston where he had a large practice until his

death in 1811. One daughter married the Hon. Wm. Allen, and another Sir James Buchanan MacAulay, a son of Dr. James MacAulay and afterwards chief justice of Upper Canada. Neither Dr. MacAulay nor Dr. Gamble engaged in private practice at York, though in their official capacity, no doubt they were called upon at times to minister to the sick of their community.

William Warren Baldwin was the first civilian doctor to settle at York—about 1800. He was a graduate of Edinburgh and had practised for a year or so in the old land before coming to Canada. The field of his professional work for a man of his energy and capacity was obviously too restricted, and as there was an insufficient number of lawyers at this time to carry on the work of the courts, Governor Hunter in 1803, designated William Warren Baldwin and three others as fit and proper persons to practise the law. "Having sprung Minerva-like at once into being in full professional maturity, these gentlemen were afterwards sometimes alluded to by less favoured brethren of the robe as the "heaven descended barristers." The various important duties which Dr. Baldwin undertook, however, is evidence of his energy, ability and versatility—characteristics which he had in common with others of the early doctors of York. He was one of the founders, later a bencher, and for many years treasurer of the Law Society of Upper Canada. An interesting incident is related of his receiving an urgent call on one occasion to attend a lady when he was pleading a case before Mr. Justice Willcocks. The latter adjourned the court and on the doctor's return inquired for the patient. On being assured of her successful *accouchement*, the less pressing judicial proceedings were resumed, thus establishing an early Canadian precedent for the pre-eminence of medicine over the law. Dr. Baldwin laid out Spadina Avenue, as a splendid approach, 160 feet in width, to the family residence, Spadina House, on the site of the present building of the Provincial Board of Health—the old Knox College. Hon. Robert Baldwin, who distinguished himself in the political struggle for constitutional government in Upper Canada was a son of William Warren Baldwin.

Intimately associated with the ruling families of that day and connected by marriage with many of the prominent families in Upper Canada, Drs. MacAulay, Gamble and Baldwin exerted a wide and salutary influence, socially and professionally on the medical interests of York and the province in general.

Dr. David Burns was one of the first settlers of York, obtaining the patent of a park lot on Dundas Street, later known as Lot Street, now Queen Street. Soon after the organization of the government, he was appointed clerk of the Crown in Chancery for the province of Upper Canada. There is no record of his having engaged in practice. His name appears in the list of subscribers to a fund for the opening up of Yonge Street, in 1801. He died in 1806, lamented as an esteemed citizen.

William Lee, a military surgeon attached to the Indian department came to York in 1807. He ministered to the Indians, making visits through the forests as far as Penetanguishene. He was relieved of his strenuous duties in 1815 and shortly afterwards was appointed Gentleman Usher of the Black Rod to the legislative council and for some years was secretary to the Upper Canada Medical Board.

Available records do not mention the names of any other doctors practising in York before 1812, but when it is remembered that it requires a community of from five hundred to a thousand to maintain the services of a physician, it is evident that the needs of the restricted field were already well supplied. When Dr. Strachan removed from Cornwall to York in 1812, the town was "only a quiet little parish" and according to Bishop Bethune the population in 1819 was less than 1,200.

There was a new-comer to York in 1812 in the person of Dr. Grant Powell, son of Hon. Justice William Dummer Powell. He had received his medical training at Guy's Hospital, and practised for three years in New York state and for five years in Montreal, where he was familiarly known as "the little doctor with the gold spectacles." He was not enamoured of practice in York, but it was well known that he took an interest in medical affairs, and was one of the first members of the Upper Canada Medical Board. He was also clerk of the legislative assembly, principal of the Court of Probate, and later judge of the Home District and clerk of the legislative council, holding the latter post until his death in 1838. His son, William Dummer Powell, died in early manhood and his widow married Dr. William Clarke of Guelph, the father of the late lieutenant governor of Ontario, Hon. Lionel Clarke, Esq.

Incidentally, it is of interest to recall the visit of Dr. William Beaumont, celebrated physiologist and pioneer in the experimental physiology of digestion, who arrived at York, April 27, 1813, not

to minister to the inhabitants, but as surgeon to the American forces attacking the town. He wrote a graphic account of the attack on York and the subsequent treatment of the wounded.

In 1814 William Dunlop, then a youth of nineteen attached to the 89th (Irish) regiment, was at York for a time and describes the place as "a dirty, straggling, village of about sixty houses, the church—the only one—being converted into a general hospital during the war." This was the first hospital at York. Dr. Dunlop afterwards went to India with his regiment, but returned to Canada in 1825 with Mr. John Galt and entered the service of the Canada Company as warden of the Forest. He was one of the founders of Guelph, and a pioneer of the Lake Huron district. As an official of the Canada Company, he was a frequent visitor and a familiar figure in York during the thirties. He was a warm friend of John Galt, author and philosopher, who as manager of the Canada Company, did much to settle the western part of the province and was ill-requited for his labors. Herculean in size, witty, kind-hearted and eccentric, Dunlop was a notable character familiarly known as the Tiger. He had considerable literary ability being a contributor to *Fraser's*, *Blackwoods* and other magazines and the author of several books. He served as member for the Huron district in the provincial legislature. An extract from his extraordinary last will and testament sufficiently indicates his peculiarities: "I, William Dunlop, of Gairbraid in the township of Colborne, county and district of Huron, Western Canada, Esquire, being in sound health of body, and my mind just as usual, which my friends who flatter me say is no great shakes at the best of times, do make this my last will and testament, etc."

He died in 1848 and the citizens of Goderich erected a monument to the memory of "a man of surpassing talent, knowledge and benevolence."

Dr. William Keating, an Irish graduate, practised in York for a short time about 1816.

He and Powell were succeeded by Dr. Christopher Widmer, F.R.C.S. (*Eng.*) a distinguished practitioner who was the first to devote his entire time to practice in York. His name is associated with every medical enterprise, and his energy, ability and foresight made him a dominating influence from the time of his arrival until his death in 1858.

Widmer was educated in London and gained a wide experience as surgeon to the 89th Light Dragoons during the Peninsular War. He came

to Canada about the close of the War of 1812 and began private practice in 1816. He was a martinet—forceful in language as well as in bearing; bluff and cavalier, but nevertheless an able, farseeing, diplomatic man and a born leader. He initiated the movement in 1817 for establishing the York General Hospital, was chairman of the Upper Canada Medical Board from 1823 until his death in 1858, was early interested in medical education, receiving students as apprentices; he was a chief mover in the establishment of the College of Physicians and Surgeons of Upper Canada (1839), and one of the founders of the medical department of King's College, (1843), besides taking an active interest in the affairs of York generally. For a time he was a member of the legislative assembly, and was one of the founders of St. Andrew's Masonic Lodge. He has justly been called the "Father of Surgery" in Upper Canada and until 1830 practically controlled the practice of York.

About 1816 Dr. Robert Charles Horne, a military surgeon came to York from Kingston where he had married a daughter of Dr. Gamble. He did not take up private practice, but became King's Printer and editor of the *Official Gazette*. After retiring from these appointments, he entered the service of the Bank of Upper Canada, but remained a member of the Upper Canada Medical Board from 1823 to 1831, and at a later date was elected treasurer of the College of Physicians and Surgeons of Upper Canada. His house was burned by order of the rebel leaders during the Rebellion of 1837, the family barely escaping with their lives.

In 1828 Dr. Peter Deihl an Edinburgh graduate (1809) came from Montreal to be associated in practice with Widmer and later became a member of the Medical Board. He married a daughter of Dr. James MacAulay. For a short time he was an attending physician to the Montreal General Hospital before coming to York.

From the foregoing remarks it will be noted that the military surgeons played an important part in the early days of the medical profession in Upper Canada. They were men of education and culture, with an excellent practical training and knowledge of the world obtained during their military service. They had received their chief education in London and Edinburgh, and some of them had studied in Paris as well.

After 1825 civilian doctors from the motherland, Canadians educated in American schools, or at McGill University in Montreal, or under the

system of apprenticeship, began rapidly to increase in numbers; nevertheless, the control and direction of medical affairs for many years remained largely in the hands of the military element. Family ties, church and political sympathies, all inclined the early doctors of York toward the party afterwards known as the Family Compact, whose dominating influence was challenged as the population of the province rapidly increased after the War of 1812.

Of 260 doctors whose biographies appear in Canniff's *History of the Medical Profession of Upper Canada from 1783 to 1850*, seventy-one were graduates of the Scottish universities, forty-three of English, twenty-eight of Irish and forty of American. Thirty-nine had their training wholly or in part under the old system of apprenticeship, ten were graduates of McGill, eleven of the Rolph School, and a few of King's College.

The estrangement of the American colonies from the motherland had an important bearing upon the subsequent evolution of the medical profession of the United States and Canada respectively which should not be overlooked. After the Revolution the tendency on the part of American graduates was to go to Paris, and at a later period to Vienna or Berlin for further study, rather than to the British schools: For this reason continental influences exercised a more powerful influence in moulding the ethics, education and practice of the American than of the Canadian profession, for medicine in Canada had its origin and received its impetus from the medical centres of the motherland—especially, London, Edinburgh, and Dublin.

The political, religious and family affiliations before noted, will suggest the causes of a cleavage in the stormy days before and after the Rebellion of 1837, in the ranks of the medical profession of York corresponding to that of the population in general.

Dr. John Rolph became an outstanding figure among the malcontents. He was the son of Dr. Thomas Rolph who came to Canada from Gloucestershire about 1810, settling in Norfolk county where he acquired a large tract of land. As a youth of nineteen, John Rolph was in York in 1812, and during the war acted as paymaster to the forces. At the close of the war he returned to England and took up the study of law and medicine concurrently, the former at the Inner Temple, the latter at Guy's Hospital under Sir Astley Cooper. He returned to Upper Canada and began the practice of both professions in Norfolk

county, though he did not pass the Upper Canada Medical Board until 1828. At first his interest centred in law and politics. In the former he rose rapidly until he was recognized as a leader at the bar; was a bencher of the Law Society of Upper Canada and his political advancement was marked by his election as Reform member for Middlesex in 1824. In 1828, being dissatisfied with a judgment of Mr. Justice Sherwood, he threw off his gown and in company with Dr. William Warren Baldwin and his son, Robert Baldwin, left the court. At this time, it is stated, he thought of entering the church but finally decided to devote his energies to medicine. He practised for a short time at Dundas but removed to York in 1831. The year after Rolph's arrival in York is notable in the medical history of the town from the fact that it was visited by an epidemic of cholera, the infection following the stream of immigration from Quebec to Montreal, Kingston and finally to York.

Dr. Strachan, who rendered notable service to the stricken population states that the epidemic raged from June to October, during which period one-fourth of the inhabitants suffered from the disease, of whom one-third died.

Shortly after Rolph's coming to York he was appointed a member of the Medical Board of Upper Canada and when the town was incorporated as the City of Toronto in 1834, he was elected an alderman. The Reformers had gained a majority in the council, and as the aldermen at that time selected one of their own number as mayor, it was expected that Rolph would have received the honour of being chosen first chief magistrate. As the result of a caucus, however, William Lyon Mackenzie was selected and Rolph resigned from the council.

One need not dwell on his entanglement in the political dissensions culminating in the Rebellion of 1837, his hurried flight, facilitated by two of his students, Henry Hoover Wright and James H. Richardson, afterwards distinguished as professors and practitioners in Toronto. He practised for six years in Rochester, when he was pardoned and returned to Toronto in 1843. The remainder of Dr. Rolph's career is intimately associated with medical education, and will be referred to later in that connection. He died at Mitchell in October, 1870, at the advanced age of eighty-three years, regarded generally in his profession as an outstanding figure, and the most brilliant teacher among the many distinguished men of his time.

The necessity for providing facilities for the training of students of medicine was in the minds of those who obtained the charter for King's College in 1827. Though for political reasons it was deemed unfortunate, yet young men of the province entering the profession of medicine were forced by circumstances to go to American schools, of which Fairfield, Geneva, Dartmouth and Jefferson were usually selected; some went to McGill after its establishment in 1824.

Christopher Widmer, John Rolph, John King and other prominent doctors of York received students as apprentices for the whole or part of their training. Rolph's capacity as a teacher was early recognized and he was urged to establish a medical school towards the maintenance of which the governor, Sir John Colborne, encouraged him with the promise of public support.

In 1834 Dr. David Lithgow, a recently arrived graduate of Edinburgh University, announced the opening of a school for the teaching of anatomy, surgery and medicine, but nothing came of this premature enterprise. The delay in the establishment of King's College, and Rolph's flight from Canada after the collapse of the Mackenzie Rebellion (1837), postponed for a time the movement for a medical school, though the College of Physicians and Surgeons of Upper Canada (1839-1841), strongly urged the necessity for action. Widmer, especially, was active in formulating plans for a medical department in King's College, and, due largely to his efforts, a teaching faculty in medicine was organized when the institution was opened in 1843.

John King was appointed professor of medicine; William R. Beaumont of surgery; George Herrick of midwifery; William B. Nicol of materia medica; Henry Sullivan was placed in charge of practical anatomy; W. C. Gwyne of anatomy and physiology and James H. Richardson was made demonstrator of anatomy. In 1845 Lucius O'Brien was appointed professor of medical jurisprudence, and E. M. Hodder was added to the staff.

On Rolph's return from Rochester in 1843 he opened a school in opposition to the newly created medical faculty of King's College, and between these institutions naturally there developed a keen rivalry. Rolph was ably supported by Dr. Joseph Workman who afterwards attained a distinguished position among the medical men of Toronto. Other members of the staff of the Rolph school were T. D. Morrison, James Langstaff, W. T. Aikins and W. B. Geikie.

In 1849 King's College was secularized and the name changed to the University of Toronto by the Baldwin Act.

In 1850 the Upper Canada School of Medicine was organized by Edward M. Hodder, James Bovell, Francis Badgley, Norman Bethune, William Hallowell and Henry Melville and soon after it became the medical department of Trinity University, which had just been established under Anglican auspices by Bishop Strachan. There were, therefore, three medical schools in Toronto in 1850: (1) the medical department of the University of Toronto; (2) the Toronto School of Medicine, commonly known as the Rolph School; and (3) the Upper Canada School of Medicine.

This multiplicity of schools naturally did not lessen the rivalry; the unhappy case of the medical student of that time is indicated in an extract from an editorial in the *Medical Chronicle* of Montreal in 1855: "Be he ever so brilliant his fate may be doomed when it is whispered that he did not attend 'our' school and his examinations cannot be begun without first discovering whose classes he followed. Rolph men sitting in judgment on the Trinity youths and the Trinity men on the Rolph youths. The ex-professors of Toronto University struggling against both parties, or joining either one as the diversion seemeth most delightful." That we have not overdrawn the subject, we quote from the correspondent: "no candidate is examined by his own teachers but by some of the other members present, who are chiefly connected with rival institutions." The editorials in the *Medical Chronicle*, however, indicate that there existed a strong rivalry, not only between McGill and the Toronto schools, but also between the medical boards of Upper and Lower Canada.

In 1853 Rolph became a member of the government of Sir Francis Hincks and due largely to his influence, the medical department of the University of Toronto was disestablished along with the other *teaching* departments in 1854. All the medical schools of the province became affiliated with the provincial university thus reorganized, which remained only an examining body after the pattern of the University of London.

The Toronto School of Medicine (Rolph's School), became the medical department of Victoria University in 1855 with a strong faculty including John Rolph (surgery), Joseph Workman (midwifery), and W. T. Aikins (anatomy).

The medical department of Trinity went out of

existence in 1856 and the same year the charter of the Toronto School of Medicine was revived by a number of doctors who organized the institution in affiliation with the University of Toronto with Edward M. Hodder as Dean.

In 1866 the *École de Médecin et de Chirurgie* of Montreal, was constituted a medical department in Quebec of Victoria University and continued in this relationship until Victoria federated with the University of Toronto in 1890.

In 1868 the medical faculty of Victoria was constituted as follows: John Rolph, medicine and pathology; Walter B. Geikie, midwifery; Walter Berryman, materia medica, therapeutics and jurisprudence; John N. Reed, institutes of medicine; John Sangster, chemistry and botany; William Canniff, surgery and surgical anatomy; John Fulton, anatomy; John King and Christopher Widmer Rolph, clinical medicine and surgery; Michael Barrett, demonstrator of anatomy; Thomas May, curator of the museum. The Victoria medical school was a strong institution until 1870 when a disagreement arose; Rolph and Geikie resigned from the staff and the faculty was eventually broken up in 1875.

The Trinity faculty was re-established in 1871, Hodder leaving the Toronto School to become Dean of the resuscitated institution and he was joined by W. B. Geikie, Norman Bethune, William R. Beaumont, William Hallowell, John Fulton, James A. Temple, Arthur Jukes Johnson, Charles Covernton, William Kennedy and McLarty. In 1878 Trinity obtained a charter as an independent teaching body, closely associated with Trinity University but affiliated with other Canadian universities. Under the leadership of W. B. Geikie, Trinity opposed state aid for medical education and a long and acrimonious controversy resulted before such assistance was finally recognized as necessary. Dr. J. A. Temple was Dean of the Trinity Medical School at the time of amalgamation.

For many years the Toronto School of Medicine continued to draw closer to the University of Toronto and finally became re-established as its medical department in 1889.

The Women's Medical College was organized by Michael Barrett who was Dean from 1884 to 1887.

It is somewhat bewildering to trace the fortunes and kaleidoscopic changes of the various schools and their university connections between 1850 and 1875 when the Trinity School and the Toronto School emerged as the only survivors of the struggle for existence in an overcrowded field.

The movement toward federation of the universities continued to gain strength and a growing appreciation gradually developed of the difficulty of adequately supporting the requirements of modern scientific training in medicine by private means; a sentiment opposed to proprietary schools with a desire to pave the way for an era of expansion, reconstruction and reorganization, lead eventually to the amalgamation of Trinity and the Women's Medical College with the medical department of the University of Toronto in 1903. This school thus constituted has become one of the largest and most important on the continent with between 600 and 700 students and over eighty of a teaching staff*.

The evolution of the medical school as an integral part of the University, the provision of modern hospital buildings, laboratories, equipment, adequate financial support, the opportunities for better staff-organization, represent the realization of the visions, the efforts and the sacrifices of men who had done their best under more primitive conditions. Those who enjoy the fruits of their labours cannot in fairness fail to recognize the good work of the old proprietary schools in training practitioners who served well their day and generation.

The recent epoch making discovery of insulin by Frederick G. Banting and his collaborators—Professor J. J. R. Macleod, Charles H. Best, J. B. Collip and others, has directed the attention of the medical world to Toronto, and is too well known to require further comment. It serves as an indication of the scientific activities of the present time, and the impetus given to medical research by the generous support of the province of Ontario, the citizens of Toronto and the Rockefeller Foundation. During the past year, under the leadership of Sir William Mulock, Chancellor of the University, a half million dollars was raised to establish the Banting Medical Research Endowment.

*Dr. R. A. Reeve was first Dean of the amalgamated institution and discharged the duties of the office at a critical period with marked ability and satisfaction.

PLAGUE IN CANADA

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It has been suggested, that some of the epidemics that occurred in Canada from time to time and which carried off large numbers of inhabitants

were true plague, and that the epidemics of 1710-1718 and 1740 were of that nature. A careful study of the epidemics of those years leaves one in doubt, as the description of the disease symptoms which prevailed during those epidemics is so meagre. There is no doubt, however, that cases of true bubonic plague have been brought to Canada by ships, and that cases of plague have been treated in the Quebec hospitals. For example: Sœur Françoise Juchereau, in her *History of the Hôtel-Dieu*, in speaking of Mlle. de Lornpré who, in the year 1648 became one of the nursing sisters, says: "It was at Nantes, in the chapel of Our Lady of All Joys, that our brave novice took her vows. She was obliged to repair immediately to La Rochelle where she was embarked. She was scarcely on board before the cross, which had made so strong an impression upon her heart, was laid upon her body in the form of a contagious disease that nearly caused her death. It was a continued fever, the most burning and most violent in the world with a girdle all around her body composed of eleven plague boils and the plague itself." She eventually recovered. The voyage lasted three months. There is no record of the importation of the disease into the country at that time. And again, in describing the death of one of the sisters during the epidemic of yellow fever in 1710 which proved so disastrous, she says: "With a burning fever she had a charbon (plague bubo). Through modesty she hid the condition for some time."

In the year 1720-1721 plague was epidemic in Marseilles and Toulon, and the Reverend Father Laure in his *Relation of the Saguenay* of that year, speaking of the sickness among the Indians of that district, tells us that "the savages attributed this species of contagion to the gods; and although we tried to undeceive them, there is nevertheless some probability that they were slightly contaminated by the plague of Marseilles. For merely on opening the bales, the clerk and some of his servants were quickly attacked by fever; and there were hardly any savages ill, except those who came to buy clothes. Moreover, some were so furious that they had to be tied. A woman in her delirium struck me a blow that made me 'see a hundred candles' as the saying is. Then, according to the custom of the savages, they were tied on their beds with their feet and hands bound to four stakes driven into the ground. As I had only a few emetics and could not attend to all, I gave a portion of them to some persons who are still living. The fear of

death alone evidently killed one, in especial. He was a robust and strong man about fifty years of age. The fever attacked him only an hour before his death. Only one man and one woman fled from their true happiness, by withdrawing, in spite of my entreaties, into the woods, where they died without any assistance."

At this time plague was very prevalent in Marseilles. It had been brought to that port in June, 1720, by a vessel from Sidon and quickly extended throughout the city and surrounding country. In Marseilles it killed 50,000. It was brought from Marseilles to Louisiana by the *Toulouse* and by the *Henry*, and spread throughout the city of New Orleans. It is very unlikely that the disease recounted by Father Laure was plague. The authorities at the time were aware of the presence of plague at Marseilles and took special precautions to prevent its entry into Canada. A quarantine was established at Isle aux Coudres and no ship from Marseilles was allowed to pass unchallenged. Only one ship came from Marseilles during that and the following year. There is no evidence of any real value to show that the disease which affected the Indians was true plague.

In the 8th of August, 1740, we read that "there arrived at Quebec Monsieur de Lauberivière on a vessel infested with plague, and the crew were in so deplorable a state that scarcely an arm could be found to manœuvre the vessel." The ship was the *Rubis*. The *Rubis* left La Rochelle for Quebec on the 10th of June, 1740. In addition to Mgr. de Lauberivière there were a number of priests and a considerable number of passengers. Shortly after it had quitted the shores of France disease broke out among the passengers and crew. "It was a continuous fever accompanied with violent headache." At the time of her arrival at Pot-à-l'eau-de-vie, (Brandy Pot), on the 27th of July, more than one hundred and sixty were sick. The crew was so weakened that the captain, M. de La Saussaye, was obliged to send a small boat to Quebec to ask the Intendant to send him fifty of the best sailors in Quebec to enable the *Rubis* to continue her voyage. The Intendant Hoquart made haste to comply with his request and a few days afterwards two vessels filled with pilots and workmen came to the assistance of the *Rubis*; one of these vessels remained with the *Rubis* and the other took the greater number of the sick to Quebec for admission to the Hôtel-Dieu. Sister Saint-Hélène, writing of their arrival, says: "I have never seen so many sick, the halls, kitchens,

parlours, everywhere is filled with sick and we can scarcely pass between the beds; all become as black as niggers as soon as they are dead." The surgeon of the *Rubis* was François Pomier, the assistant surgeon Monsieur Chevalier. M. Nicolas le Clerc, the surgeon of the *Minerva*, rendered aid. M. Gignos, the assistant surgeon of the *Minerva*, also gave aid. M. Paul Lajus, who gave assistance, died. He was twenty-five years of age. There were two hundred and forty-one admitted to the hospital and twenty-eight deaths. It is very questionable if the disease was plague. One would expect a higher death rate. One is rather inclined to think of typhus. The low death rate leaves the impression that the sick were pretty well cared for in the Hôtel-Dieu in those days. Our modern hospitals could scarcely show a better record.

During the summer season of 1756 six vessels of the King arrived on which there were a great many sick, and in the history of l'Hôpital Général we read that "Father Floque was the chaplain of the *Léopard*, one of the king's vessels which was the most infected with plague." And again, "the vessel, the *Léopard*, arrived plagued with a disease more serious inasmuch as it became epidemic." The disease continued until February, 1757. Some of the soldiers from this ship proceeded to Montreal, where they fell ill and were admitted into l'Hôpital Général. The disease spread throughout the hospital and the city, causing many deaths. The symptoms described in the history of l'Hôpital Général—agonizing pain, faces swollen and unrecognizable, death in four or five days—rather incline one to think of hæmorrhagic small-pox. The evidence, however, is incomplete, and final conclusions of the nature of the disease cannot be drawn.

In the years 1906-1907 plague was prevalent on the Pacific coast, particularly in the cities of Seattle and San Francisco; two cases developed in Vancouver and one in Victoria. The case in Victoria was that of a stevedore who undoubtedly contracted the disease while working on board an infected ship. The origin of the two cases in Vancouver could not be traced; one was that of a young girl and the other that of a labouring man. At the time it was felt that the Chinese and Japanese were a great source of danger and it was recommended "that they be made to live more in conformity with our manner of living."

At the time quarantine regulations were put in force and well carried out. Provision was made for examining rats at the provincial laboratory,

and a fee was paid for each rat brought in. A special concrete building was erected for the purpose. As plague appeared from time to time in California precautions were taken by the Hon. Dr. H. E. Young, provincial health officer of British Columbia, and his associates, to prevent its entrance into Canada.

PRACTISING UNDER DIFFICULTIES

Members of the medical profession have not always enjoyed the social standing now almost universally conceded to be theirs. The road by which they have travelled has not been without incident or milepost; the eminence now occupied has been attained by gradual progress from beginnings most inauspicious. Precisely how inauspicious these beginnings were we sometimes fail to appreciate and the discovery comes as a surprise, if brought to light when delving among the records of the past.

A source of information which might easily be overlooked in connection with this matter is Nicholas Denys' book on North America, one of the first of a long series of publications intended for colonization propaganda, the last of which has not been written. His book was published in Paris in 1672.

A practical fisherman, whose acquaintance with the most intricate details of all branches of the business in which his countrymen held a prominent place, he has transmitted to us in a most detailed manner the procedure followed by the French fishermen of his age. The picture of the position held by the doctor in the enterprise merits the noting.

French vessels were accustomed to leave their home ports in the early Spring on their way to the selected fishing grounds. If they were not engaged in the Bank fishery their crews numbered about fifty or more to the vessel. A doctor was one of these, or at least there was an individual who combined with medical duties those of assistance to the cook or steward, barber, mentor of the staff of boys or apprentices, throater at one of the splitting tables, shoreman and gardener, and whom Denys refers to as the *chirurgien*.

The boys or apprentices usually numbered from four to six or more. The duty of keeping them in order, admonishing them when unruly, spurring them to action if a disposition to laziness

ness was apparent and wielding the cat if milder measures failed was part of the doctor's labours. The medical care of the crew naturally fell on him. Perhaps there was but a short transition from this to attending to the tonsorial requirements of the crew.

Arrived at the fishing site in some protected harbour on the coast line, a number of varied tasks awaited the voyagers, of which the task of catching and curing the fish for the return cargo was but one. The ship had to be stripped in order that the sails might be used for the cover of the huts in which the men lived. Boats must be built, largely from material brought from France. A wharf, sheds and fish flakes must be constructed from timber cut near at hand. The doctor and his apprentices here found their hands and time occupied, for the transportation of the material used in these structures fell on them.

Already, too, many weeks may have been passed in the close confinement of the small vessel, on a diet little conducive,—as experience had taught—to continued health. Therefore, having arranged for more commodious quarters on shore, it was necessary to supplement the ship's stores by food procured by trapping and shooting, or by that which might be grown and reach maturity in the short time the stay on the coast permitted. The doctor must not only prescribe a change of diet, but he had to procure it, by shooting or trapping animal food, or by raising the garden produce in which safety and health depended.

Other duties he might not overlook, those connected with his assistance-ship of the cook. It was with no dainty appetites that the evening meal was attacked, after many hours of arduous work on the part of those actually engaged in fishing, and who had set out at the break of day for the fishing grounds. Moreover, there was the important task of diluting the wine to a correct degree. On ordinary days the dilution was half and half, but if the day had been an especially difficult one, if the task of dressing the fish had protracted itself well into the night, or

under special circumstances, wine of full strength had better be used. The important matter was to have some on hand for the homeward journey in the fall.

Meanwhile, the task of curing the fish brought in by the boats was that of the shoremen of which the doctor was one. He had to take his place as throater at one of the splitting tables, where it might take almost all the night to clean up the catch of the day. The shoremen attended to the details of the drying and curing process, spreading the fish on the flakes or on the beach, turning them when necessary, covering them if fog or rain threatened injury, or piling the cured product for packing in the vessel when ready for the homeward passage. There was oil to be extracted and barrelled for shipment. There were other by-products to be looked after. Between assisting the cook, flogging the apprentices, weeding his garden, shooting fresh meat required for about fifty men and aiding the shoremen and practising his profession the doctor's time was pretty well occupied.

He was paid by being given with the others a proportion of the profits of the enterprise. To the crew went one quarter of the value of the fish caught and of this he had his share with the others. He had been given the equivalent of \$50.00 or \$60.00 at the first of the voyage with which to buy his medical chest and the medicines required. If any drugs were left over at the end of the trip, he was permitted to keep them and the chest itself. In addition each man paid him about 20 sols for barbering, which helped, since his share with the rest of the crew might vary considerably, the average being between \$40.00 and \$50.00 for a trip of many months duration. We do not know how many signed on for a second trip.

Those acquainted with the jargon of the Gloucester bank fishermen will remember that the cook of the vessel is almost universally referred to as the "Doctor". Is this an echo of the custom of their French confreres of several hundreds of years ago?

A. C. J.

Medical Societies

THE MAJOR PROBLEM OF PUERPERAL SEPSIS*

Streptococcal infection of the placental site, is the usual cause of puerperal sepsis. Two out of every five cases of puerperal fever due to the *Streptococcus pyogenes*, succumb to the infection. As this organism does not normally inhabit the genital tract, the question, which forms the basis of this address, "How did it get there?" is raised.

Septic infection of the placental site may be either, (1) extrinsic, i.e., organisms alien to the patient, introduced either during or after labour by intrauterine or vaginal manipulation and instrumentation. Or (2) intrinsic, i.e., the organisms existing in the tissues of the patient at the time of labour. These organisms may be conveyed to the placental site by manipulation, or may be carried there by the blood stream.

Lockhart noted that 18.9 per cent of women, whose vaginae harboured streptococci before labour, developed puerperal sepsis, while only 1.9 per cent of those in whom streptococci were not isolated, did. Certain individuals have a chronic infection, the organisms residing either in the sinuses, gums, tonsils, urinary tract or intestine. Every healthy person carries in the intestine, bacteria which are potentially virulent, but the woman in whose faeces streptococci predominate, runs a greater risk of infection than if the colon bacillus were in the ascendancy. Their resistance to the streptococcus is low, hence any injury, even birth trauma, goes hard with them.

It is thought that in the majority of cases, the infection is conveyed. The perianal skin always abounds in organisms which, unless the greatest care is exercised will be carried into the vagina during any manipulative procedure. That the infecting organisms usually are conveyed in this manner, is strengthened by the fact that the colon bacillus is often found with the streptococcus in the uterine contents.

Puerperal sepsis may be prevented, (1) by proper surgical technique, sterile towels, instru-

ments, gloves, etc., (2) by abolishing all septic foci before labour, (3) by sterilizing the perineum before delivery. As the abolition of all septic foci is impossible, the problem is to prevent these organisms entering the vagina. Blair Bell is of the opinion that coitus in the last few weeks of pregnancy, may convey organisms into the vagina, which may later cause sepsis. The perianal region should be covered with a sterile towel during delivery and the entire perineum painted with some strong non-irritating antiseptic. The gloved hand should also be anointed with a similar antiseptic so that if any organisms are carried up during the manipulation, they get a lethal dose in transit. Violet green is suggested as efficient and satisfactory. Vaginitis, whether streptococcal or gonorrheal should be treated to a cure before pregnancy is advised, but if the two co-exist, the infection should be rigorously cared for, in spite of the pregnancy. In cases of severe vaginitis occurring at term, Caesarean section may be the safest means of delivery. If the uterus is infected, hysterectomy is to be considered.

Serums and vaccines, although they have to date not proven very satisfactory, are worth a trial where streptococcal infection is especially to be feared.

ELEANOR PERCIVAL

MEETING OF THE HALIFAX BRANCH OF THE MEDICAL SOCIETY OF NOVA SCOTIA

FOCAL INFECTION AND SYSTEMIC DISEASE

The Halifax Branch of the Medical Society of Nova Scotia held a joint meeting with the Halifax Dental Society, on the tenth of February. Papers were presented by two prominent members of the Dalhousie faculty of dentistry, Drs. W. W. Woodbury and J. S. Bagnall. The discussion which followed was shared in by both physicians and dentists, who were a unit in their opinion that the interchange of views was most instructive, and in their hope that such joint meetings will be held frequently in the future. Dr. Woodbury's paper, which was illustrated by lantern slides and blackboard drawings, dealt very comprehensively with anomalies

*Victor Bonney, *The Lancet*, Jan. 10, 1925. An address given at the Windsor & District Medical Society.

of the teeth and associated parts. After pointing out the very natural approach to mouth deformities on the part of dentistry in the past from the standpoint of tooth relationship, Dr. Woodbury showed that this approach was in reality ultra-mechanical unless modified by a comprehensive view of the field of science in which the whole problem lay. The paper comprised a partial survey of this field. Sir Arthur Keith was quoted at some length to demonstrate that from an evolutionary standpoint marked changes of an easily measurable magnitude had occurred in the British race since shortly before the Norman Conquest. At that time the "edge to edge" bite of the incisors was practically universal. It is now very rare, the overlap being considered normal. The fact was stressed that tooth relationship was in no sense static, but an expression of the sum total of the metabolic forces acting on the teeth. The suggestion of the embryologist that certain well defined dental malrelations are an expression of early developmental inhibition was noted. The question of etiology was briefly discussed showing that the then satisfactory but rather dogmatic handling of hereditary and environmental factors of twenty-five years ago, was no longer tenable in view of our larger knowledge of the mechanism of inheritance. The bearing of variation, especially its more functional phase as expressed in correlative variation, was noted, together with Cuvier's principle of harmonious development. After pointing out the necessity of considering habit as a natural property of living matter before thinking of its pathological aspect, the paper went on to discuss the vital importance of as full knowledge as possible of the great field of growth and development and closed with a brief reference to the many problems suggested by a study of the physiology of the oral tissues. Dr. Bagnall discussed the interrelationship between dental focal infections and systemic diseases. Attention was directed not only to fistulous openings leading from root fragments, infected apices, etc., but also to the

various degrees of periodontoclasia and to impacted teeth. Reference was made to various studies undertaken to determine if chronic dental infections produce changes in the blood picture, none of which have revealed a means of establishing a definite diagnosis, so that up to the present time proof that diseased teeth are the cause of systemic conditions often cannot be secured previous to extraction. The x-ray is often of great assistance, but a negative picture does not necessarily mean that a tooth is not menacing health. Slight roughening of the root outline is of more significance than a large clear area which indicates that infection is being walled off. In each case consideration must be given to the disease from which the patient is suffering, the resistance of the patient, the x-ray or other available diagnostic evidence relative to the tooth, the possibility of successful treatment of the tooth and the possible effects of extraction on the mechanics of mastication. In a case of grave illness, any reduction of a toxic condition may be of service and the extraction of a suspicious tooth may therefore be justifiable. Sacrifice of teeth without due consideration of possible results is to be deplored. The effect of injudicious extraction on the masticatory mechanism may be more serious than that of a localized infection. Investigations now being made indicate that under suitable conditions offending teeth may be treated so as to remove any menace to the general health. In determining whether or no such treatment should be undertaken, the pros and cons should have the same consideration as any other clinical problem. In conclusion, Dr. Bagnall made the plea that, when time permits, oral cleanliness should be secured before undertaking surgical operations—especially those on the alimentary tract, and that the diet of children should be arranged with reference to sufficient tooth-building elements and foods which will give the exercise requisite to normal development of the maxillæ.

W. H. HATTIE

Abstracts from Current Literature

MEDICINE

The Treatment of Tuberculous Peritonitis by Oxygen Inflation. Hayes, E. W., *Amer. Rev. of Tuberc.*, 1926, vol. xiii, p. 27.

This form of treatment has been used before, and Dr. Hayes thinks it should be given more consideration. Whilst he does not say that it is a cure-all for tuberculosis in closed cavities, he believes that the method is the simplest and most efficient and that it greatly shortens the period ordinarily required for treatment. The ordinary surgical procedure of opening the abdomen in tuberculous peritonitis, and exposing the contents to the air for varying lengths of time, has its best results when the disease is localized, but these results may be improved by the additional employment of air or oxygen in inflating the abdomen.

Several writers are quoted as reporting excellent results in the treatment of tuberculosis of closed cavities by means of the inflation with oxygen, and Dr. Hayes has used it at the Los Angeles General Hospital for the last three years. He has used it chiefly in tuberculous peritonitis and enteritis, but also reports two cases of abscess in which it was employed with success. In his experience it has produced strikingly beneficial results. Even in the more severe types of tuberculous peritonitis, with or without exudate, granting that the general condition of the patient was fairly good, or the lung condition not too active, this method often effected a cure when other methods failed. In the ulcerative type of tuberculous enteritis, it is often of great value in relieving symptoms, and if given in the early stages may be curative.

The technique he has used has been the same as that followed in artificial pneumothorax. The skin is rendered aseptic and is anesthetized with novocain. The site for the introduction of the needle is about one and a half inches to the left and below the umbilicus. In ascitic cases the fluid is first withdrawn through a trocar. The amount of oxygen used varies to some extent with the case. Dr. Hayes found that between 300 and 800 c.c. was the most beneficial quantity. The treatments were given at intervals

varying from a few days to two or three weeks; it depended on the condition of the patient.

H. E. MACDERMOT

Diabetes: Electrocardiographic Studies. Blitzsten, E. P. W., and Schram, D. L., *Arch. Int. Med.*, December, 1925.

Studies were undertaken to see in what way electrocardiographic tracings of diabetic patients differ from those of normal persons of the same age and sex.

Electrocardiographic tracings of diabetic patients showed notching of the main deflections more often than tracings of other subjects of the same age and sex. The higher the blood sugar concentration, the more frequent the notching, and as the sugar concentration decreased the notching tended to disappear. This notching was not due to a bundle branch lesion. Since there was a reduction in the notching with decreased sugar content it seemed probable that there was an improvement of the myocardial condition. It required several weeks of low sugar concentration to cause any marked change in the notching.

As the sugar content of the circulating blood increased there was an increase in the height of the Q-R-S wave in the electrocardiograms, while a decrease in the sugar content caused a smaller swing of the galvanometer string. The P wave also showed definite changes in height of excursion.

Following ether anesthetization, dogs showed a marked and fairly constant hyperglycemia. The electrocardiograms showed an increase in the height of the main deflection as soon as the dog was under the influence of ether and relaxation was complete.

Since changes in blood sugar concentration seemed to produce definite changes in the action current, the authors suggest that the sugar acts directly on the cardiac muscle as a protoplasmic poison.

LILLIAN A. CHASE

Postural Hypotension. Bradbury, S., and Eggleston, C., *Amer. Heart Jour.*, 1925, vol. i, No. 1.

This is a report of clinical and pharmaceutical observations on three patients whose blood

pressure showed extremely wide variations with changes of posture. There is no close agreement as to what readings represent hypotension: some place it at 110 systolic pressure, others say 100, and readings of as low as 81 and 90 have been reported in apparently normal individuals. It is well recognized, however, that the posture of the patient causes a more or less definite change in the blood pressure. In rising from the supine to the erect posture there is in general, a fall in the systolic and a rise in the diastolic pressure, but this, although definite, is usually small.

In the cases under consideration the variations in blood pressure consequent on change of posture, were extraordinarily wide. In one case the systolic reading was 40 standing, 42 sitting, and 105 lying down and frequently the pressure while standing was 35; in another case a typical reading was 158 lying flat, 100 sitting and 52 standing. In the third case readings were noted of 84 in the lying position to 45 in the sitting. Elevating the foot of the bed brought about equally striking variations in the pressure.

In each case there was a persistently slow heart action which was accounted for (in the absence of any evidence of heart block) by impairment of the sympathetic accelerator control of the heart. Atropin gave rise to no cardiac quickening, and there were none of the typical responses to adrenalin such as vasoconstriction, and this suggested an extensive disturbance in the functional activity of the vegetative nervous system. Further evidence of this disturbance lay in the absence of sweating which was not affected even with the higher levels of pressure.

On the other hand, epinephrin did cause some temporary heightening of blood pressure, although it did not check the tendency for the pressure to vary with position.

No treatment seemed to be of any avail in these cases. The methods tried included the administration of thyroxin, epinephrin, dried suprarenal substance mixed glands, strychnine and digitalis and the enforced consumption of sugar and water.

H. E. MACDERMOT

The Diagnosis of Early Nervous Disease.
Blandy, M. A., *Lancet*, Dec. 19, 1925.

The importance of a careful case history is emphasized. Neurologists often find that some

early but important symptom has been overlooked, such as transient double vision or weakness of a limb.

The first sign of disease of the nervous system may be a psychological one such as change of disposition, even in such conditions as intracranial tumour, cerebro-vascular disease, disseminated sclerosis, encephalitis lethargica, and cerebrospinal syphilis.

During her six years tenure of registrarship at the National Hospital for Paralysed and Epileptic at Queen's Square, Miss Blandy had abundant opportunity of observing the symptoms of brain tumour, and was impressed with temperamental changes characteristic of tumours in various regions of the brain. Patients with large frontal tumours are apt to be slow and dull; in case of smaller tumours, witty and facetious. Patients with temporo-sphenoidal tumours are generally facile, pleasant people undisturbed by their alarming symptoms such as headache and dimness of vision. Temperamental changes in other organic diseases of the nervous system are also noted; the smiling euphoria of disseminated sclerosis, the psychic changes following encephalitis lethargica even as late as two years after the illness, and the mental symptoms of confusion and depression sometimes found in subacute combined degeneration of the cord.

Miss Blandy lays stress upon quick appreciation of the outward details of a patient's appearance and manner, since diseases of the nervous system are much more objective than diseases of other systems of the body. Slight changes in gait and facial expression must not escape notice. Subjective symptoms are also very important. A slight impairment of some acquired skilled movement may be apparent to the patient only. A sense of fatigue in the legs and aching on exertion may precede the objective signs of neuritis by several weeks. Fits may be the first intimation of organic disease such as brain tumour, and disseminated sclerosis.

In conclusion, Miss Blandy protests against the expression "nervous break-down". In her experience this has been applied to very many undiagnosed organic diseases.

A. G. MORPHY

SURGERY

Pre-Operative Treatment of Urinary Obstruction. Hunt, Verne C., *Surg., Gyn. and Obst.*, Feb., 1926.

In the early days of prostatic surgery little was known of the effects of obstruction. Within recent years reliable function tests have been devised and the practical application used. Therefore the management of the prostatic patient embraces a great deal more than the surgical removal. Prostatic obstruction is most common between sixty and seventy-five years of age, and not only the age but the coincident cardiovascular changes and the accompanying renal insufficiency makes the patient a substandard risk. The causes of death are (1) pre-existing and co-existing organic disease, (2) surgical accidents, (3) post-operative complications.

Acute urinary retention may at times require surgical drainage, but prostatectomy is never an emergency procedure, just as in intestinal obstruction, the relief of the urinary obstruction is the thing of prime importance. Renal insufficiency, cardiovascular disease and chronic pulmonary lesions are responsible for 50 per cent of the deaths following prostatectomy. Hence their treatment is essential.

The phenolsulphonephthalein test and blood urea estimation are reliable indexes of renal function. Likewise the salivary urea estimation is reliable. These tests should be repeated to note progress, and treatment continued until the tests indicate approach to normal conditions. The electro-cardiograph is useful not only to determine the reserve of the heart muscle but also as to prognosis.

It is imperative that drainage be instituted to improve these patients. The author prefers catheter drainage to suprapubic cystotomy, thereby eliminating the two-stage operation. In his experience less than 6 per cent of patients are intolerant to an indwelling catheter. The catheter drainage allows a one-stage operation, and at this operation visualization of the operative field and accurate hæmostasis can be carried out. The death-rate at the Mayo Clinic in a series of 1,783 cases was 5.5 per cent. The rate for the two-stage operation was 7.5 per cent, and the one-stage 4.8 per cent. A complete review of the deaths shows that "the mortality

rate following prostatectomy on the best surgical risks without preparation approaches closely that of the exceedingly poor risks requiring cystotomy, and is twice that following preparation of patients by urethral catheter drainage." The period of drainage is for ten days or longer.

R. V. B. SHIER

Treatment Following Operations for Gastric and Duodenal Ulcer. Eusterman, George B., *Surg., Gyn. and Obst.*, Feb., 1926.

The author asserts in his introductory remarks that with the marked increase in our knowledge of physiological effects and of the complications of various diseases, active co-operation between internist and surgeon is demanded. This is particularly true in the condition under discussion. The chief cause of poor surgical results is incomplete examination. A careful history, a radiological examination by an expert, and an analysis of gastric contents must supply the facts on which to construct a diagnosis.

The gastric analysis not only proves retention but also the presence or absence of achlorhydria or achylia. The syndrome of ulcer may be simulated in so-called achylia gastrica. Anacidity in the presence of radiological deformity characteristic of ulcer may mean (1) an inactive, healed, malignant, or syphilitic lesion; (2) an association of various diseases ranging from chronic cholecystitis to pernicious anæmia; (3) an asthenic neurotic state.

In well-selected cases there is little need for post-operative supervision. However, when symptoms do occur they are either functional or organic. The former respond to medical supervision. The primary ulcer may not have healed, or may have been reactivated by stomachal irritation. There may be motor disturbances from mechanical causes, and recurrent lesions. The author makes a strong plea for dietetic control following gastric operations. While not favouring the making of an invalid out of the patient by too strict dietetic measures, yet there is need for some commonsense control. From four to six weeks is the length of time recommended for dietetic measures, or until healing is complete. There is a healing ulcerated surface at the site of an anastomosis for two weeks. In cases of hyperacidity the usual Sippy diet is recommended until this healing is com-

plete. Following this general directions in booklet form are given each patient. The ill-effects of tobacco are pointed out. R. V. B. SHIER

PÆDIATRICS

Enlargement of the Spleen in Measles. Bleyer, Adrien, *Amer. Jour. Dis. of Chil.*, January, 1926, vol. xxxi, p. 26.

The author reports the results of examination for splenic enlargement in four hundred cases of measles. He notes that pædiatric and general medical text books differ greatly on this point, and also that the clinicians and pathologists differ in their views. Bleyer found that of forty-seven patients with measles, who were examined the day before the rash appeared, the spleen was found to be enlarged in 2 per cent. Of fifty-eight patients examined on the first day of the rash the percentage rose abruptly to 24, of eighty examined on the second day the spleen was palpated in 43 per cent, or almost twice the number of positives encountered on the first day, it being quite often as large again as it was on that day. Sixty-five patients were examined on the third day of the rash and enlarged spleens were found in slightly more than half. On the fourth day there were forty-nine patients with a percentage of positives of 52, the spleen being of about the size noted on the third day and reaching commonly 1, 2 or even 3 cm. below the ribs. On the fifth and sixth days of the rash the spleen was less readily palpable, and was felt in only 25 per cent of cases. During the convalescence the spleen was palpated at or below the costal margin in only 15 per cent of cases.

The time of enlargement preceded the time of appearance of complications, such as otitis or pneumonia, and is found in those diseases, in the absence of measles, in only 6 and 13 per cent respectively. The severity of the disease was not found to bear a relationship to the size of the spleen. The author concludes that splenic enlargement is directly related to the virus of the disease and should be included in the symptomatology of the disease. R. R. STRUTHERS

Diphtheria following Tonsillectomy. Local Resistance and General Immunity to Diphtheria. Zingher, A., *Amer. Jour. Dis. Chil.*, January, 1926, vol. xxxi, p. 72.

The difficulty of differentiating the post-operative sloughing membrane, seen in the throat following tonsillectomy, from that of a true diphtheritic infection superimposed on the traumatized area, is a very real one. The purpose of this paper is to emphasize this danger, to indicate the necessity of taking nose and throat cultures before operations on these structures, and to protect positive diphtheria carriers by a prophylactic dose of antitoxin.

Reports of three children who developed diphtheria of the pharynx or larynx after tonsillectomy are given. When these three factors, absence of general immunity to diphtheria—as shown by a positive Schick test—presence of virulent diphtheria bacilli in the nose or throat and a local tissue injury, such as an operation, come together, diphtheria is quite certain to follow, and the disease is likely to prove serious because of the early and rapid absorption of a fatal dose of toxin from the extensive raw surface. Even in the presence of a positive Schick test a person may harbour virulent diphtheria organisms in the throat, without actually developing the disease, due to the presence of a local tissue immunity in the throat. This local immunity is destroyed by the local tissue damage and the clinical disease develops. Such a local immunity may be present also toward scarlet fever, which may be broken down by the presence of another disease, such as diphtheria. Dr. Zingher, who speaks from a vast experience, advises strongly that preliminary nose and throat cultures for diphtheria bacilli be taken as a routine before tonsil and adenoid operations. If the cultures are positive a prophylactic dose of 1500 units of diphtheria antitoxin should be injected, unless the patient has already been tested with the Schick test and shown a definite negative or negative pseudo-reaction.

R. R. STRUTHERS

Association Notes

THE VICTORIA MEETING, JUNE 21ST TO 25TH, 1926

The stage is set for a big week in Victoria in June. The details of a splendid programme of entertainment are being arranged by a large committee of enthusiastic members of the Victoria profession, and a Ladies' Committee under the leadership of Mrs. Forrest Leeder, has busy days planned for all the doctors' wives and daughters in Canada if they will but accept the invitation and make the journey to Victoria and Vancouver Island in June. The Entertainment Committee is captained by Dr. Hermann M. Robertson, and Dr. Stuart G. Kenning is its energetic secretary.

The Council will meet on Monday June 21, and will be luncheon guests of Dr. Forrest Leeder. Dinners, luncheons, dances, drives, garden parties, receptions, golf, riding, bathing at the Crystal Garden Pool, in the lakes and at the beaches; yachting, canoeing, fishing, tennis, bowling and mountain climbing for the more energetic, will fill in every portion of all days which the scientific programme does not occupy.

The British Columbia Medical Association annual dinner will be held on Tuesday, June 22, and will be followed by music and dancing.

On Wednesday the official opening will be carried out on schedule time, with brief addresses from Dr. David Low of Regina, President, and Dr. Forrest Leeder, President-Elect of the Canadian Medical Association. The lieutenant-governor of British Columbia, the Hon. Robert Randolph Bruce; the Hon. John Oliver, premier of the province and J. Carl Pendray, Esq., mayor of Victoria will each extend a welcome to the members of the combined Associations.

The scientific programme will then commence, and the present draft of the programme is worthy of any national convention. It is intensely practical, and we are fortunate in the personnel of our speakers.

Luncheons will be held each day in the Empress Hotel where it has been arranged that all the meetings will take place.

The Ladies' Committee is busy providing for the lady visitors but the full announcement regarding these counter attractions will not be published until the scientific programme is completely

arranged. We may state, however, that Mrs. Leeder is planning a reception at her home "Stoneyhurst" on Rockland Avenue, to follow a delightful drive for the lady visitors along the Marine Highway, where all the water is salt and all the air is fresh. June is the month of roses and Victoria excels in roses, and the gardens will all be in full bloom. There will be other drives; one especially to show where the big timber from which British Columbia fir is cut. A short but delightful drive takes one to Esquimalt Harbour where the new dry dock, one of the very largest in the world, should prove of interest. All ladies will be provided with cars for the trip by applying at the Information Desk.

On Wednesday evening, the annual dinner of the Canadian Medical Association will be held in the Empress Hotel. If it is over early, and the ladies are not at the Crystal Garden, or at some other function, a visit may be arranged to the parliament buildings, where Premier Oliver and his ministers will greet all the guests. These fine buildings contain much of interest. A visit can also be arranged to the great observatory on Saanish Mountain where other worlds can be seen through one of the largest telescopes in this world.

As the lieutenant-governor of the province has only recently arrived from England it has not yet been possible to interview him, but it is hoped that a dance can be arranged at Government House some evening after dinner; a garden party, however, has been planned by the Ladies' Committee for Friday at Government House, which members of the Association may attend after the scientific programme is ended.

On Thursday, June 24, there will be no papers after three o'clock, to permit of a drive to Butchart's Gardens. These are the wonderful sunken gardens at the home of Mr. and Mrs. R. P. Butchart on Tod Inlet; their unique splendour should be seen. A visit will also be made to Brentwood College on Brentwood Bay, where tea will be served. This is another beauty spot where nature has been most lavish.

On Thursday night the Canadian Medical Association dance will take place at the Empress Hotel.

On Friday, after the Receptions and Garden Party at Government House plans are under way,

for Alumni dinners and receptions under the charge of Committees representing McGill, Toronto, Dalhousie, Queen's, London and Winnipeg and all other groups who may wish to hold reunions on that night. (It is understood that there will be no penalties for behaviour of the medical student type, but the management of the hotel request that no old inter-college feuds be revived and no old time student rushes be staged). There may also be a smoker or a dance. The Committee states that the only time the orchestra will not play is at the Scientific Meetings.

Victoria urges you to make this your vacation and stop over to see all the things there are to see in and around Victoria and on Vancouver Island. The trip up the island leads one into innumerable possibilities for holiday making. One may go to Cowichan Lake or Cowichan River to fish for trout, or try Brentwood which is nearer for grilse. A visit also to Qualicum Beach Hotel will place you in reach of good fishing and bathing; there is also an excellent golf links overlooking the sea.

A trip to Campbell River and Forbes' Landing will repay every fisherman, and the big timber is a superb awe-inspiring sight. Sproat Lake and Great Central Lake near Alberni are also well worth a visit. All this information, with numerous photographs and maps will be placed at the disposal of visitors and plans should be made to do the things properly. It is hoped that the only disappointment our visitors will experience will be lack of time to see all the beauties of this western Island which is rapidly growing in popularity as the playground of the Pacific Northwest.

The profession in Victoria are sparing no effort to make this 1926 meeting a grand success. There are, however, a few things each member must do to assure its success and his comfort.

HOTEL ACCOMMODATION

Advise as early as possible (which should be at once), Dr. Gordon C. Kenning, 1207 Douglas Street, Victoria, B.C., what hotel accommodation you require.

Do not neglect to make your reservations promptly. This is important as tourist travel is very heavy in Victoria. Be sure to bring with you your wife, your daughter, your golf clubs, your fishing rod and tackle, and your bathing suit.

HOTEL ACCOMMODATION

Empress Hotel—European Plan Only

Single Room, without bath \$5.00 per day
“ “ with “ \$6.00 per day
Double Room, without bath \$8.00 per day
“ “ with “ \$10.00 per day

Dominion Hotel—European Plan Only

Double Room, without bath \$4.00 per day
“ “ with “ \$6.00 per day

Strathcona Hotel—European Plan Only

Single Room, without bath \$2.00 per day
“ “ with “ \$3.00 per day
Double Room, without bath \$3.00 per day
“ “ with “ \$4.50 per day

Glenshiel Hotel

Single Room, without bath \$1.50 per day
“ “ with “ \$2.50 per day
Double Room, without bath \$2.50 per day
“ “ with “ \$3.50 per day up

(Also operates on American Plan)

James Bay Hotel

Single Room, without bath \$2.50 per day
“ “ with “ \$3.00 per day
Double Room, without bath \$3.50 per day
“ “ with “ \$4.00 per day

(Also operates on American Plan)

Balmoral Hotel—European Plan Only

Single Room, without bath \$1.50 per day
“ “ with “ \$2.50 per day
Double Room, without bath \$2.50 per day
“ “ with “ \$3.50 per day

Metropolis Hotel—European Plan Only

Single Room, without bath \$2.00 per day
“ “ with “ \$3.00 per day
Double Room, without bath \$2.50 per day
“ “ with “ \$4.00 per day

Douglas Hotel—European Plan Only

Single Room, without bath \$1.50 per day
“ “ with “ \$2.50 per day
Double Room, without bath \$2.50 per day
“ “ with “ \$3.50 per day

While the Convention Meetings are to be held in the Empress Hotel, the Hotels Committee desires to state that all hotels listed are within three or four blocks of the Empress Hotel.

LISTER MEMORIAL FUND

Dr. F. N. G. Starr, chairman of the Lister Memorial Club advises us that the following additional contributions have been received:

Adam Wright, Toronto \$10.00
Medical Society of Nova Scotia \$300.00

This brings the total subscriptions received to date to \$4,651.00. The objective is \$5,000.00.

Will all correspondents to the *Journal*, including Provincial Editorial Boards, please note that apart from original articles, all material for publication must be in the hands of the Editor, not later than the fifteenth of the month preceding month of issue. This will insure early publication of each number.

Miscellaneous

SUNLIGHT TREATMENT: ARTIFICIAL AND NATURAL

The value of artificial and natural sunlight is now generally recognized. Ultra-violet ray lamps may now be found in the offices of so many physicians that the following directions for the use of such artificial and natural light rays, which have been given by Sir Henry Gauvain, medical superintendent of the Lord Mayor Treloar Cripples' Hospital and College at Alton, Hants, may prove of value. Care must always be exercised at the commencement.

1. No new patient is to be exposed until he is acclimatized and insolation ordered.
2. The patient's head must always be protected by a canopy or sun hat.
3. The patient must never be allowed to become too hot or too cold. If he complains of the heat, his bed or stand must immediately be put in the shade; if he is faint a cold compress to be applied to the cardiac region and the medical officer on duty summoned. If he appears cold or shivers he is to be instantly covered, hot bottles applied, and current switched on if he occupies electrically heated bed.
4. Blistering the skin must be always avoided. Excessive erythema (redness) or any blistering to be immediately reported.
5. In commencing treatment, as a general rule (usually individual instructions will be given) parts of the patient's body may be exposed as follows (five, ten, or twenty minutes hourly means an exposure for either of these periods in three separate hours):

First day—Legs to knees for five minutes hourly.
Second day—Legs to knees for ten minutes hourly.
Third day—Legs to groin for ten minutes hourly, and where possible turn patient and treat other side of body as on first day.
Fourth day—Expose to groin and buttocks for ten minutes hourly. Total exposure twenty minutes hourly.
Fifth day—As on fourth day, and in addition one aspect of trunk exposed for five minutes hourly.
Sixth day—As on fifth day, and in addition other aspect of trunk exposed for five minutes hourly.

Seventh day—As on sixth day, but double exposure of trunk permissible.

Eighth day—Total exposure of trunk twenty minutes hourly permitted and exposure of legs to be increased.

Subsequently, periods of exposure may be gradually increased if the patient is pigmenting satisfactorily. When pigmentation is fully established, the patient may be completely exposed for increasing periods until he can tolerate continuous exposure, which may now be undertaken whenever sunshine is available up to a total of three hours daily, and to a limited extent even in the absence of direct sunshine. Certain cases will be found in which these rules cannot be rigidly followed, and less exposure is called for or more exposure may be tolerated. Individual instructions will be specially given for these patients.

6. If unsuitable weather supervenes which interrupts treatment, insolation must be resumed at the earliest possible moment. If pigmentation is fully established, half the exposures last given may be permitted.

7. Sinuses or ulcers should be exposed for as long as and whenever possible, as soon as pigmentation is established. Any purulent discharge must be immediately swabbed. If there are flies about or it is windy and there is any dust, sinuses or ulcers must be touched with a little iodine. The iodine is to be confined to the sinus and not swabbed over healthy skin.

8. Even in the absence of sunshine, discharging wounds on the face, neck, and extremities are to be exposed unless contrary directions are given. Dressings in these situations should be applied only at night time, or if the patient remains in the ward.

9. In any case where a patient's evening temperature exceeds 100° F., the patient must not be exposed the following day unless special orders are given.

10. A daily record should be kept of the period of exposure of each patient.

11. Patients who do not pigment, or who freckle, are to be reported and are not to continue insolation unless specially ordered.

12. Under no circumstances may a nurse leave the patients in her charge while they are receiving sun treatment.

NOTE.—It is desired that pigmentation of the skin be secured as speedily as is safely possible. That pigmentation must be maintained and intensified whenever weather conditions permit, with due regard to the above rules. These rules refer to May sun in the southern counties. At other seasons and in other districts they require modification.

Contamination of Apples by Arsenic.—A few weeks ago we referred to the prosecution of a dealer for selling apples containing arsenic, and explained briefly how it is that arsenic is sometimes present on the peel of this fruit. A circular issued by the Ministry of Health on December 21st states that this matter has been brought to the notice of the Minister. Considerable quantities of arsenic have been found on the surface of certain imported apples, and two cases of arsenical poisoning have been

traced to the consumption of imported Jonathan apples; samples of these apples which have been examined have shown various amounts of arsenic ranging up to 1/10 grain per pound. The contamination of apples by arsenic has been occasionally reported for a number of years, but the quantities of arsenic found by analysis on former occasions have generally been insignificant, and until recently no cases of illness have been traced to the consumption of such apples.—*Brit. Med. Jour.*, Dec. 16, 1925.

Obituaries

Alexander MacNeill, M.D., C.M., F.A.C.S., passed away on February 6, 1926. By his death the medical profession of Prince Edward Island suffered a distinct loss.

Dr. MacNeill was born at Canoe Cove, Queens County, P. E. Island on Feb. 17, 1853. He attended Prince of Wales College and then took his medical course at McGill graduating with honours in 1883. The inspiration of such teachers as Osler and Ross made a lasting impression upon him, and did much to make his career a successful and brilliant one. He spent his first fifteen years at Kensington, P.E.I.; but after post-graduate work, he settled in Summerside where he spent his last twenty-seven years. He leaves to his profession the worthy example of a careful and zealous physician and surgeon of great ability and energy. He kept himself abreast of his profession in its great development during the past twenty-five years by means of much post graduate work, and gave generously of his time and experience to many medical associations of which he was a leading and influential member. He was a past president of the P.E.I. Medical Association and a member of the Medical Council of Canada in which he was honoured by his appointment to its presidency. He was a Fellow of the American College of Surgeons, and a regular attendant at its meetings and particularly active in the maritime section of which he was a past president. He was the senior member of the staff of the Prince County Hospital and one of its founders, and his active interest meant much in its success.

Dr. MacNeill was taken ill in December last and went to Montreal where he was operated on, but the operation revealed an incurable and hopeless condition which progressed to a fatal ending. It was characteristic of Dr. MacNeill that he lectured to the nurses' training class the night before he left for Montreal. It may be truthfully said that he died in harness; his name will long be a household word in this province where "Dr. Alex" as he was familiarly called was so widely known and universally and justly respected.

The interment took place at Summerside with full Masonic honours.

Dr. MacNeill was married to Miss Emma Bowness of Kensington who with one daughter Miss Jean and a son Frank survive him.

Two of Dr. MacNeill's brothers are members of the medical profession, Dr. J. F. MacNeill of Summerside and Dr. J. W. MacNeill of Battleford, Sask.

W. J. MACMILLAN

John Gray McKendrick, M.D., LL.D., F.R.C.P., (Ed.), F.R.S., Emeritus Professor of Physiology in Glasgow University died in Glasgow on January 2nd. He was born in Aberdeen on August 12, 1841. Neither of his parents, who died very young, could he remember. About the age of thirteen he was taken to Braco in Perthshire to stay with his paternal grandfather, who was factor on the estate of Braco.

Here for a whole summer he herded sheep from five in the morning to eight at night. He had his breakfast and his dinner of porridge brought out to him on the braes of Braco; and by the end of the season he had saved one pound. He had no books to read; but he was not lonely for he had for companions, the snipe, the curlew and the sky-lark, and for a moving picture, the silent lights and shadows on the peaceful grassy slopes of the Ochils.

While he was serving his apprenticeship with a

law firm in Aberdeen, he was advised to attend the meeting of the British Association in that city in 1859. Here he saw for the first time Faraday, Owen, Murchison and Huxley: already science had begun to call him. As in so many other cases, the road thither lay through a medical training. After rising many a morning at five and studying until the office opened at ten, young McKendrick passed the "Medical Preliminary" at Aberdeen University in 1861. He found it impossible, however, to serve two masters, so law was abandoned, the study of medicine begun at the University of Edinburgh and a living was eked out by evening work in the office of "The Daily Review."

He heard Goodsir lecture, and saw Turner and Joseph Bell demonstrate. His struggles were pathetic: he had to "coach" in anatomy, but he took Goodsir's medal in 1863. His teachers in Edinburgh were the giants of those days; James Miller, the surgeon and ardent advocate of temperance; Simpson and Syme, whose controversy was at its height, and Laycock of the Chair of Medicine who forestalled German psychoanalysis by about seventy years.

Long afterwards, he summarized his medical course—"no laboratories, no apparatus, no histology, no bacteriology, and seven different theories of inflammation."

After some months at the Infirmary at Chester where he saw 200 cases of smallpox, McKendrick obtained the position of surgeon to the Eastern Dispensary, Whitechapel, at £100 a year without board. But he afterwards accepted a position in the newly built Belford Cottage Hospital at Fort William, Invernesshire. Here in the serene purity of Glen Nevis with plenty of time for study, he returned to his favourite zoology. In 1867 he was married to Miss Mary Souttar of Aberdeen. It was in Lochaber in 1869 that McKendrick accidentally met Hughes Bennett who suggested his becoming one of his assistants at £100 a year in the vacancy created by William Rutherford having gone to the Chair of Physiology at King's College, London. Hughes Bennett had introduced the study of Histology into Edinburgh University; and McKendrick's duty was to teach this subject.

Bennett's health had been failing, and he spent each winter session from 1870 to 1873 on the Riviera so that McKendrick had sole charge of his class during that time.

Bennett had left him the legacy of lecturing to the first physiology class in Edinburgh that was composed solely of women. McKendrick thus became a pioneer in the famous movement for the higher education of women, whose activities for so long disturbed the academic doves. The well-known Miss Jex-Blake was one of his students. Amongst the men he taught were Sir William Watson Cheyne, Professor Cash, Professor Ewart, and Sir George Beatson.

In 1873 Bennett resigned his chair, and Rutherford was recalled to fill it. McKendrick's position at this time was embarrassing; he had had the best of reasons to expect to succeed Bennett; he had a house and young family in Edinburgh, and—nothing a year.

He at once offered a course of forty lectures to women only, of whom 150 were enrolled. He was appointed to the extra-mural lectureship of physiology at Surgeon's Hall, and also to that at the Dick Veterinary College, Clyde Street.

Here it was he met James Dewar with whom was begun that joint research which ended in the discovery of the electric current produced in the retina and optic nerve as the result of light falling on the eye. The account of this was published in the Proceedings of the Royal Society of Edinburgh for 1873. For the

first time a current of action had been demonstrated in a sensory nerve as the result of the normal stimulation of its end-organ.

Curiously enough almost at the same time, Holmgren in Upsala made the same discovery, but this was entirely unknown to the two Scottish workers. In 1871 McKendrick was elected to the Fellowship of the Royal College of Physicians of Edinburgh, and shortly afterwards to that of the Royal Society of Edinburgh.

Dewar and McKendrick also investigated the physiological action of quinoline and certain pyridine bases: this was one of the first researches which correlated chemical constitution and physiological action. Through the kindness of Joseph Bell, McKendrick was enabled to visit the continent of Europe in 1872 for Bell suggested that his friend might accompany a patient, and so the two set out for Germany where McKendrick met Max Schultze, Pflüger, Du Bois-Reymond, Ludwig and Helmholtz.

In 1876 the chair of the Institutes of Medicine at Glasgow fell vacant by the resignation of Dr. Andrew Buchanan. It was in the gift of the Crown, and McKendrick was appointed. He found a lecture-room, a sphygmograph, a few old microscopes and some diagrams; on these he built up the Department of Physiology which preceded the present Institute of Physiology presided over by Professor D. Noël Paton, F.R.S.

Dr. McKendrick was one of the most pleasing of lecturers; his discourse had all the smoothness of a well told tale: he contrived to make even the driest part of his subject interesting. Indeed so popular was he that he received numerous invitations to lecture in Glasgow and neighbourhood.

In 1881 he received the honour of the appointment of Fullerian Professor of Physiology at the Royal Institution. In this capacity he delivered a number of the Friday evening discourses on such subjects as the respiration of fishes, the internal ear, vocal tones and the electric fishes. In subsequent years he gave eight lectures on the History of Physiology, some on muscle and still others on the senses. He also delivered a course of the famous Christmas lectures to children. All this involved a very great deal of travelling from and to Glasgow. In 1882 McKendrick received the honour of the degree of LL.D. from his Alma Mater; in the same year he attended the Canadian Meeting of the British Association, and on the way home visited a number of American cities.

At Glasgow, McKendrick acted for some years as Secretary of the Philosophical Society of Glasgow, and subsequently filled the Presidential chair.

In 1884 he was elected into the Royal Society and later served on the Council. He held examinations in Physiology at London, Oxford, Cambridge, Liverpool, Leeds, Manchester and Aberdeen.

McKendrick found time to write a large number of articles, obituary notices, biographies, and more than one text-book.

His written works have the same pleasant flavour as his spoken words. To the *Encyclopædia Britannica* he contributed the articles on Nervous System, Ear, Eye, Senses, Stereoscope and Longevity. In 1878 he published his "Outlines of Physiology," and ten years later his "Text-book of Physiology," splendidly illustrated in two volumes. In 1899 his "Life of Helmholtz" in "The Masters of Medicine" series appeared—a condensed but excellent account of the work of the great German mathematician and physiologist.

Physiological acoustics had always interested McKendrick; and from about 1892 onwards he investigated the nature of the traces made on the wax cylinder of

the phonograph. Later he was enabled to devise a method for eliminating the hissing sound which so mars the music as reproduced by that instrument. McKendrick was very fond of music; and no account of his life would be complete which did not refer to that and to his love of poetry and to his fondness for animals. Early in his career he had written a song, "A Cowie Fisher Lassie," which was set to music by Sir Herbert Oakley the Reid Professor of Music at Edinburgh.

Dr. McKendrick is survived by two sons, Dr. J. S. McKendrick of Glasgow and Colonel Anderson McKendrick, M.D., I.M.S., (retired), Director of the Laboratory of the Royal Colleges, Edinburgh, and by a daughter, the wife of Dr. A. A. Warden of Paris; his other daughter, who was married to the Rev. R. Bruce Taylor, D.D., Principal of Queen's University, Kingston, Ont., died some months ago. D. FRASER HARRIS

As we go to press we have just learned with extreme regret of the sudden death of Professor A. R. Cushny, M.A., M.D., LL.D., F.R.S., Professor of Materia Medica and Pharmacology in the University of Edinburgh, formerly of the University of Michigan, and editor of the well known textbook of Pharmacology, and of important monographs on Digitalis and on Urinary Secretion. We shall refer to his life work at greater length in the May issue.

Dr. Peter McNaughton, medical superintendent of the Ontario Hospital for the Insane died in Brockville on March the 5th. Dr. McNaughton had been associated with the Ontario institutions for the insane for many years; he was the vice-president of the Ontario Neuro-Psychiatric Association.

Dr. Hugh K. Hyndman, one of the best known of the Huron county physicians, died in Exeter on March the 6th in his eighty-third year. In spite of his advanced age Dr. Hyndman had been practicing practically up to the time of his death, and he had been in active service in Exeter for upwards of forty years.

Dr. Henry Wallwin died in Barrie on March the 1st. Born sixty-six years ago in Vespra township Dr. Wallwin had practiced medicine in Barrie for thirty-five years. He was a member of the Board of Education and chairman thereof for one year. With all his active practice he had kept in touch with civic politics and served four terms as alderman and was chairman of the fire and police commission.

Dr. Wallace Smuck, of Toronto, who for thirty years had practiced in that city died on March 6th after an illness of over two months. Dr. Smuck was born in Ancaster and graduated from the University of Toronto in 1893. During the war he was officer in charge of the Givens Street branch of the Toronto Base Hospital; he also served as senior medical officer at the Polish military camp in Niagara Falls.

Dr. J. U. Lalonde died at his residence, 585 Lasalle Road, Verdun after an illness of several years. He was born at St. Etienne de Beauharnois, sixty-three years ago. He was educated at Montreal College, Sherbrooke Street and took his medical course at Laval University. Deceased was provincial revisory medical officer for the Catholic Order of Foresters and also consulting physician for La Sauvegarde Insurance Company. He founded the Goutte de Lait of Ste. Cunegonde and that of Ste. Irene, and took great interest in questions of public health.

Medical News from the British Empire

GREAT BRITAIN

Our London Letter

(From our correspondent)

Unqualified Practice

The public interest in unqualified practice still continues. The fog which threatened to settle on the lay mind in regard to this matter has been somewhat dispelled by a debate in the House of Commons on February 9th which was opened by Dr. Graham Little, the representative in Parliament of the University of London.

Dr. Little asked for an authoritative enquiry with the object of making recommendations to Parliament for dealing with the whole subject of irregular practice in medicine and surgery.

Dr. Little said that the spread of unqualified practice in the British Empire on the part of osteopaths, chiropractors and other irregular practitioners was on the increase. The lay press has fostered an unhealthy interest in irregular practitioners largely because Mr. Herbert Barker has been a very skilful bonesetter and has been knighted. Dr. Little was of the opinion that one of the causes of the rapid growth of unqualified practice was the length of the medical training at the present day. This result was wholly unforeseen when the medical course was lengthened to six years as it now is. Speaking from prolonged personal experience, Dr. Little said that much harm was done by the optician who was not an oculist and by the "quack" dentist fitting plates to septic stumps. The public is labouring under the mistaken idea that the General Medical Council is persecuting osteopaths; whereas the fact is that it can take no cognizance of them at all, for the very reason that they have no qualification which are registrable.

Professor L. Sinclair, the only member of the General Medical Council who is also a member of the House of Commons, made this clear in the debate and told the House that it could not consider the registration of osteopaths since it had no means of inspecting their schools of instruction which are in America. One of the

duties of the Council is to inspect the medical schools whose degrees it registers. Possibly by the end of the century the public will have begun to understand this.

Dr. Graham Little reminded the House that in the United States osteopaths were not allowed to hold commissions in the medical services of the Navy or Army. He did not misrepresent the basic contention of the osteopaths that all diseases arise from some malposition of the vertebrae of the spinal column, and that therefore all treatment must essentially consist in manipulating the vertebral column and the emergent nerves. Stated in these words, this conception of the causation of disease is hopelessly inadequate. For one thing, it leaves out of account the invisible, micro-organic sources of many of the greatest scourges of past or present, and in particular of syphilis, tubercle, malaria and cancer.

What benefit is to be derived from the manipulation of the bones and joints in syphilis, tubercle, malaria or cancer only the transcendental intuition of an obsessed osteopath could explain. We have known of a tubercular joint being manipulated until it became disorganized and had set up disseminated tuberculosis, and an abdomen massaged for a gastric ulcer until the patient died of internal hæmorrhage. The public which cannot protect itself must be protected from that little knowledge which so often is so dangerous. England, Germany and five Australian States were the only countries of the civilized world which did not penalize unqualified practice.

Dr. Drummond Shiels made some valuable contributions to the debate. He pointed out that as osteopathic manipulations constituted a very small part of the remedial measures of surgery, it was absurd to contemplate issuing a general diploma to practice medicine and surgery on the ground of having been instructed in bone-setting. He assured the House that the General Medical Council had no pleasure in striking a name off the register; and that

the Council really suffered from a lack of publicity in regard to its doings.

Professor Sinclair explained that if it served any good purpose, lay members could be sent to the Council both by the Privy Council itself and by the Universities. There is some likelihood that this will be done.

The Minister of Health, Mr. Neville Chamberlain, said that he had no wish to minimize the dangers of unqualified practice: those he regarded as two-fold, direct and indirect, the former being those from injudicious manipulations, and the latter being the risk of restraining a person from going early to the only kind of physician who could give a reliable and properly reasoned diagnosis.

Mr. Chamberlain knew of nothing to prevent

the British osteopaths from founding a College in this country and granting their diplomas.

Lord Dawson of Penn recently made the excellent suggestion that medical men might, in many cases, employ more generally especially trained technicians who were not themselves medical men but who could, under expert supervision, carry out the mechanical details of certain treatments.

It is significant that the lay interest in irregular practice does not extend to that of the legal profession. We do not notice any widely expressed desire to have our wills made by unqualified lawyers, nor have we noticed any requests to be sentenced to death by an amateur judge.

D. FRASER HARRIS

London, March 1st, 1926.

SOUTH AFRICA

We have commented before on the movement in South Africa for the formation of a South African Medical Association distinct from the South African Branch of the British Medical Association. The South African medical journals now give us in detail the discussions that have been taking place on this matter consequent on a visit of Dr. Alfred Cox, General Secretary of the B. M. A. The expression of views has been perfectly frank, and it is interesting to note that frequent reference was made to the development of the Canadian Medical Association as distinct from branches of the British Medical Association in Canada. A definite section of the South African medical profession, as far as we can gather, is in favour of a separate local association, and yet it is quite clear that they also have a strong desire to keep some sort of connection with the British Medical Association, something corresponding with the status of affiliation existent between the Canadian Association and the B.M.A. In opposition to this group are those who still belong to the Branch

Society and are keenly desirous of retaining that organization as it is.

The result of a combined meeting of the profession at Johannesburg in December, 1925, was the adoption of certain resolutions which read as follows:

"(1) That this meeting recognizes the urgent necessity of the medical profession in South Africa being united in a single organization.

(2) That in forming such an organization full reciprocal consideration would be given to the interests and susceptibilities of existing organizations.

(3) That it be a recommendation of this meeting that the two Associations should meet to discuss the proposal made to-night that a South African Medical Federation (B.M.A.) be formed with the object of obtaining the above objects."

It is of course fully realized that the existence of two separate medical organizations in South Africa as at present, is a source of weakness to the profession as a whole which must be overcome by every effort possible.

AUSTRALIA

UNIVERSITY OF SYDNEY

As successor to the late John Irvine Hunter who occupied the chair of anatomy, the Senate has appointed Associate Professor A. N. Burkitt. Professor Burkitt graduated Bachelor of Medicine in University of Sydney with first class honours in 1916 during which year he also took the degree of Bachelor of Science. He entered the service of the University in 1919 as Lecturer and Demonstrator in Anatomy and on the recommendation of the late Professor Hunter he was promoted in July, 1924, to the grade of Associate Professor. At this time he was prosecuting his studies in histology and other branches of anatomy in Europe. Dr. Burkitt's

appointment to the Chair was recommended by a Committee of Advice in England consisting of Professors J. T. Wilson and Elliot Smith, after it had been ascertained that Dr. Davidson Black was unable to accept the Chair.

Dr. Burkitt has a wide acquaintance with all branches of anatomy and anthropology and possesses abounding enthusiasm as an anatomist. He has proved himself to be a keen student of research and a man of considerable scientific gifts of knowledge and insight. His appointment to this important Chair should prove a happy link to the new Department of Anthropology shortly to be established by the University.



UNIVERSITY OF WESTERN ONTARIO MEDICAL SCHOOL, LONDON, ONT.

News Items

ONTARIO

ONTARIO MEDICAL ASSOCIATION MEETING, LONDON, MAY 25, 26, 27, 28, 1926

The preliminary programme which follows speaks for itself. From a post-graduate point of view here is an opportunity for an intensive three-day course in general medicine that will attract the man who is willing to combine a short holiday and a "refresher" course. Surgery and its handmaiden gynaecology are the last sections to complete the programme but they have been arranged in a very inviting way. Our old friend the right upper quadrant will occupy two papers. The acute abdomen in the child will be given differential diagnosis. The hand in its infections will be simplified. Fractures will come in for attention in a unique way. Plastic surgery of the face will be reviewed in a lantern demonstration; while the significance of genito-urinary symptoms will be explained.

In obstetrics the progress toward ideal management will be reviewed, the toxæmias explained, the prophylaxis of injuries indicated and the rôles of gynaecological surgery prescribed during the child bearing period.

The London men are hard at work making every arrangement that will effect a successful meeting, and they look forward to having a large gathering of their Ontario confrères on the occasion of the first meeting in London.

The programme for the ladies entertainment will be ample to insure that their visitors will not find time heavy on their hands; for everyone there will be opportunity to enjoy the pleasure of visiting the show places of London, the Forest City, at the most delightful time of the year.

PRELIMINARY PROGRAMME

PLACE OF MEETING—Masonic Temple.

TUESDAY, MAY 25TH

Morning and afternoon sessions of the Committee on General Purposes.

Tuesday evening—Round Table Dinner and Conference conducted by the Committee on Inter-Relations.

WEDNESDAY, MAY 26TH

9:00 a.m.—General Registration.

Report of the Committee on General Purposes.

"Diagnosis of Common Skin Conditions", (lantern), Dr. G. G. Campbell, Montreal.

"Early Manifestations of Insanity," Dr. G. H. Stevenson, London.

"Cardiac Diseases", Dr. A. McPhedran, Toronto.

Discussion on papers presented.

12:30 p.m.—Luncheon.

Ontario.

2:00 p.m.—"Surgery of the Right Upper Quadrant", Dr. J. B. Deaver, Philadelphia.

"The Oral Administration of Glucose", Dr. R. D. Rudolf, Toronto.

"Streptococcus Infections", Dr. W. L. Holman, Toronto.

"The Etiology of Pyorrhœa", Dr. J. H. Fisher, London.

"Fibrositis", Dr. Chas. Hunter, Winnipeg.

Discussion on papers presented.

7:30 p.m.—Annual Dinner-Dance, Ontario Hospital.

THURSDAY, MAY 27TH

10:00 a.m.—"Non-Tuberculous Pulmonary Affections", Dr. T. McCrae, Philadelphia.

"Acute Abdomen in Children", Dr. C. M. Carruthers, Sarnia.

"Résumé on Fractures—Views of the Western Ontario Academy of Medicine", Dr. G. A. Ramsay, London.

"Choice of Anæsthetics", Dr. Wm. Webster, Winnipeg.

Discussion on papers presented.

12:00 noon—Business meeting.

2:00 p.m.—"The Rôle of Gynæcological Surgery in the Child Bearing Period", Dr. H. M. Little, Montreal.

"The Significance of Signs and Symptoms in Genito-Urinary Diseases", Dr. J. W. Hutchinson, Ottawa.

Symposium—"Headache"—

Accessory Sinus Factors, Dr. R. H. Skillern, Philadelphia.

Neurological Factors, Dr. Foster Kennedy, New York.

Ocular Factors, Dr. G. E. de Schweinitz, Philadelphia.

Discussion on papers presented.

7:30 p.m.—Alumni Dinners.

FRIDAY, MAY 28TH

10:00 a.m.—"Reconstructive Surgery of Face Including Hare-Lip and Cleft Palate", (Lantern Slides), Dr. F. Risdon, Toronto.

"The Radiological Diagnosis of Lesions in the Right Upper Quadrant", (Lantern Slides), Dr. L. R. Hess, Hamilton.

"Obstetrical Injuries, their Pre-

vention and Treatment", (Lantern Slides), Dr. R. Ferguson, London.

"Progress in the Past 35 years Towards the Attainment of Obstetrical Ideals", Dr. C. B. Oliver, Chatham.

"The Pneumonias of Childhood", Dr. E. A. Morgan, Toronto.

Discussion on papers presented.

12:00 noon—Business meeting.

12:30 p.m.—Luncheon.

2:00 p.m.—"Prognosis in Relation to Diseases of Kidney and Liver", Dr. L. Rowntree, Rochester, Minn.

"Toxæmias of Pregnancy", Dr. Stephen Langevin, Montreal.

"Acute Infections of Hand—Surgery, Pathology and Treatment", Dr. D. Wigle, Windsor.

"Chronic Intestinal Indigestion in Children", Dr. R. R. MacGregor, Kingston.

Discussion on papers presented.

PROGRAMME FOR THE LADIES

Wednesday Afternoon—Garden Party at "Windermere"—Residence of Dr. Hadley Williams.

Thursday Afternoon—Garden Party at the Ontario Hospital.

RELAXATIONS

Golf—Three Splendid Courses.

The programme does not take up the whole day—plenty of opportunity is offered for a game, so bring along your clubs.

Motor Trips—To London's Beauty Spots.

Western University.

Springbank Park.

Ontario Hospital.

Queen Alexandra Sanatorium.

Westminster Psychopathic Hospital.

Port Stanley (by Electric Line).

University of Western Ontario Convocation Week—University Play—Convocation.

Alumni Reunions and Dinners.

Inspection Visits—To Western Medical School and London Hospitals.

On February 17th, the Hamilton Medical Society was addressed by Dr. J. J. R. Macleod on the subject, "The physiology of insulin." At a later meeting of the same Society held on March 10th, Dr. Geo. A. Ramsay of London gave a talk on "Fractures-non-operative treatment; Thomas Jones and other splints of war development," illustrated by lantern slides.

The North Bay Medical Society met on February 17th, Dr. A. A. Fletcher of Toronto gave a talk on "Diet and Insulin in the treatment of diabetes mellitus."

At a meeting of the Sault Ste. Marie Medical Society on February 19th, Dr. Roscoe Graham of Toronto gave an address on "Surgical emergencies in the gastrointestinal tract."

On February 25th, Dr. A. J. Grant of Western University Medical School, London, addressed the members of the Brant County Medical Society on "Local anaesthesia, its uses and limitations."

The North Waterloo Medical Society met in Kit-

chenor on February 26th, listened to an address by Dr. R. I. Harris of Toronto on "Tuberculosis of the bones and joints," with lantern slide illustrations.

At a meeting of the Essex County Medical Society held in Windsor on March 2nd, Dr. C. Stewart Wright gave a paper on "Chronic arthritis."

The Renfrew County Medical Society met in Pembroke on March 11th, addresses were given by Dr. J. K. M. Dickie and Dr. R. S. Steven of Ottawa.

The twentieth anniversary of graduation of the class of '06, medicine, University of Toronto, will be celebrated on June 1st. All members are requested to kindly send their postal addresses to the secretary of the year Dr. D. Kilgour, 70 Gerrard St. E., Toronto.

Dr. Oskar Klotz, professor of pathology and bacteriology at the University of Toronto, has been granted six months leave of absence to engage in research on yellow fever at Lagos, West Africa, with the Rockefeller Foundation. N. B. GWYN

GENERAL

INTERNATIONAL TUBERCULOSIS CONFERENCE

The Fifth Conference of the International Union against Tuberculosis will be held at Washington, on September 30th, October 1st and 2nd, 1926. The following are the subjects chosen for discussion:—

Clinical subject.—"The part played by contagion in tuberculosis among adults." Reporter: Professor Gaetano Ronzoni, of the University of Milan.

Biological subject.—"Anatomical structure of tubercle, from histogenesis to cavity." Reporter: Dr. Allen Krause, Baltimore.

Social subject.—"Tuberculosis and milk." Reporter: Dr. Wm. Park, New York.

In addition a public address will be given by the President of the National Tuberculosis Association, Dr. Theobald Smith.

In virtue of Article IV. of the By-laws, all councillors and ordinary members of the Union are invited to the Conference, of which they are members by right. Moreover a third category of members mentioned under the last paragraph of Article IV. of the By-laws as "Members of the Conference," will be admitted to the Conference on the recommendation of the national anti-tuberculosis association of their respective countries, or, in certain cases, on the recommendation of their national government, when the latter is a member of the International Union. "Members of the Conference" will be expected to pay a subscription of five dollars.

We are requested by Dr. A. Grant Fleming, Chairman of the Child Hygiene Section, Canadian Council on Child Welfare, to state that the Canadian Council on Child Welfare have published a series of pre-natal letters. These letters were prepared by qualified physicians. The letters are designed to give general practical information and advice, and to urge the need and value of early and regular supervision by the family

physician. The letters will be distributed through the Provincial Health Departments to any woman requesting them. Further information and a specimen copy of the series will be sent to any physician who will make application either to his Provincial Health Officer or to the Canadian Council on Child Welfare, Ottawa.

NATIONAL HEALTH CONGRESS TO MEET IN TORONTO, IN MAY

Three great health organizations in Canada are combining forces to hold a unique national health congress in Toronto early in May, plans for which are now almost completed.

This congress will represent the joint strength and points of view of the Ontario Health Officers Association, the Canadian Public Health Association and the Canadian Social Hygiene Council. It will last from May 3rd to 7th and will be addressed by many notable health officials from the various Canadian provinces as well as by famous medical experts from Great Britain and the United States. The annual meetings of the Canadian Public Health Association and of the Canadian Social Hygiene Council will be held during the Congress and there will be sectional conferences of laboratory Workers, Public Health Nurses, Child Hygienists and Social Hygienists.

By special arrangement the Academy of Medicine, Toronto has invited all the visiting physicians to meet with them at the Academy on the evening of May 6th where the question of "Periodic Health Examination" will be discussed from both national and international angles.

Other matters of great interest to the general public which will be dealt with by the congress will be "Medical Aspects of Immigration" and Immunization against Disease" one of the latest phases of preventive medicine.

NOVA SCOTIA

Drs. Clement MacLeod, of Halifax, and J. A. Milne, of Woodburn, have returned home after a period of study in England and on the continent.

The vocational building of the Nova Scotia Sanatorium, Kentville, was destroyed by fire in the early

morning of March 2nd. There was no one in the building at the time the fire originated, so the loss was in property only.

The Halifax Society of McGill Graduates held its annual dinner meeting on the evening of February 26th,

when Drs. A. T. Bazin and F. H. MacKay, of Montreal, and Hon. Dr. W. N. Rehfuess of Bridgewater were present as guests. Dr. Bazin and Dr. MacKay responded to the toast to old McGill, and Dr. Rehfuess proposed a toast to Student Days.

On the casting vote of the chairman, Dr. W. D. Forrest, the Halifax city health board has amended the by-law governing the sale of milk, and this commodity may now be obtained either "loose" or in bottles at the option of the purchaser. The action of the health board provoked a vigorous discussion, in which the press participated on what appeared to be party lines. In the endeavour to check what it regarded as a reactionary movement, the Massachusetts-Halifax Health Commission engaged Drs. W. Grant Fleming and R. St. J. MacDonald, of Montreal, to investigate the milk supply of Halifax and report thereon. The report of these gentlemen will be awaited with interest.

In the February number of *Public Health Notes*, the Provincial Health Officer sums up the vital statistics for the provincial year which ended September 30, 1925. The crude death rate was 11.6; the standardized rate 10.2. During the five year period 1908-1913, the average number of deaths per year was 7,337. Last year the number was 6,078—a betterment of about four per day. The birth rate for the year was lower than in the previous year, but the number of infants surviving was larger. The infant mortality rate was 78.8. Death from tuberculosis (all forms) numbered 603; which represents a rate nearly 10 per cent less than that of the previous year. Deaths from non-pulmonary forms of tuberculosis, however, exceeded those of the previous year by 35 per cent. The experience in respect of diphtheria, measles and typhoid fever was again favourable, these diseases accounting for but twenty, four, and twenty-four deaths respectively. On the other hand, whooping cough ranked next to tuberculosis in the specific death rates; while cancer reached a new high level and caused forty-five more deaths (542) than pulmonary tuberculosis (497). The maternal death rate was also high, six per thousand births. While these exceptions to an otherwise very favourable report are to be regretted, the general improvement over preceding years is remarkable. Although the death rate has been falling for several years, the returns for last year show the most gratifying improvement which has thus far been recorded.

At the annual meeting of the Halifax Visiting Dispensary, held on the eighth of February, the reports presented showed that this old institution continues to serve the necessitous people of Halifax in a most commendable way. The removal of the Dispensary from its former location to the Dalhousie Health Centre has proved advantageous. The Dispensary, while relinquish-

ing its out-patient clinics to the University, retains its visiting medical service and continues to dispense medicines, surgical dressings, etc., to poor people upon the recommendation of any physician. It has recently shared with the Victoria General Hospital in the purchase of 200 additional milligrams of radium, of which the Dispensary's share will be in the custody and at the service of the Hospital.

The report on Humane Institutions shows a total of 17,319 admissions during the year. Of the provincial institutions and the local general hospitals a very satisfactory report is given. Few of the county institutions for the insane are described as satisfactory, and the same may be said of several of the almshouses.

The annual reports of the Provincial Health Officer, recently presented to the legislature of Nova Scotia, contain much that is of interest to medical men. In that dealing with the public health, evidence is presented of steady and effective progress. A comparison of the counties shows that the greatest statistical improvement has been effected in those counties in which public health nurses are employed. The communicable diseases in general were kept well in hand, sporadic outbreaks having usually been prevented from assuming epidemic proportions. Efforts for the control of venereal diseases are being sustained through treatment clinics, hospitalization when necessary, treatment by private practitioners in districts not served conveniently by clinics, and educational measures. The press is being used for educational purposes, and health exhibits are shown at county exhibitions, etc. Anti-tuberculosis work goes on, with more vigorous prosecution in the counties in which there are public health nurses. The tuberculosis diagnostician held many clinics in various parts of the province and examined 1,123 persons. The superintendent of nursing service is utilized, as far as practicable, to offset the lack of public health nurses in many counties. The nurses working under the supervision of the provincial department examined 18,555 school pupils, while nurses working under local educational authorities examined 18,163. Of course this represents but a small part of the activities of these helpful ladies. At the various clinics, apart from those for venereal diseases, nearly 2,000 new cases were received. At the laboratory, 8,753 specimens of various kinds were examined.

To the several gaols of the province there were admitted 1,803 persons, of whom only 146 served gaol sentences exceeding two months, although eighty-seven were transferred to the maritime penitentiary. Conditions in many of the gaols are far from satisfactory. The desirability of a prison farm to serve the needs of the three maritime provinces is set forth in the report.

W. H. HATTIE

NEW BRUNSWICK

Dr. D. R. Moore of Stanley, N. B. is slowly recovering from an operation for double cataract. Dr. Moore has been in poor health for some time. The news of his recovery is welcomed by his many friends throughout the province.

Dr. W. E. Rowley, Saint John, has been confined to the General Public Hospital for three weeks; the result of a fracture of the tibia and fibula of his right leg. His progress has been excellent. The Doctor's misfortune has entailed the usual amount of suffering but he has escaped travel over winter roads through the worst part of the year. This year, the roads are

really bad even in the city, owing to heavy snow fall and steady cold weather.

Dr. Sormany of Shediac and Dr. Nugent of Saint John, acting for the executive of the New Brunswick Medical Association this week addressed a circular letter to the profession in the province informing them of the proposed series of meetings to be held throughout the summer at various centres to take advantage of extramural lectures provided for in the scheme of the Canadian Medical Association. It is proposed to follow a schedule similar to the one worked out in Ontario. These meetings are only feasible in New Brunswick during

the summer, as winter conditions forbid successful gatherings during the winter months.

At the next meeting of the Commission of the Jordan Memorial Hospital at River Glade, a proposition will be presented for the expenditure of considerable new money for the enlargement of this institution. At the present time, there is a large waiting list of tubercular patients requiring treatment at River Glade for whom there is no accommodation. Both the Saint John County Hospital and the River Glade Institution are filled to capacity. The good work done at both places should be the greatest factor in determining the further expenditure of money along these lines.

Since the first of the year the bed capacity at the Saint John Public Hospital has been crowded beyond its limits. Both the main building and the annex, for contagious diseases, have been constantly filled. The need for further accommodation is most evident and a movement is now on foot to provide a new wing with special accommodation for maternity cases. This movement has the aid of the local women's organizations, and has long been recommended by the local physicians.

On February 23rd, Saint John was again privileged to entertain a team of lecturers from Upper Canada. Dr. A. T. Bazin of Montreal General Hospital, presented a scholarly and interesting paper on Gall Bladder Disease; its diagnosis and treatment. Dr. F. H. McKay from Montreal General Hospital, read a paper on Cord

Tumours. Both these papers were the subject of considerable discussion; much information was elicited both from the papers and from the discussion. These gentlemen also appeared in two other centres in New Brunswick; before the Fredericton Medical Society and the Moncton Medical Society. The attendance at all these meetings was exceptionally good in spite of most severe weather.

At Campbellton on March 10th at the Town Hall, the graduation exercises of the second class from the Soldier's Memorial Training School was held. Addresses were delivered by His Honour, Judge McLatchy, Chairman of the Board of Management and the address to the graduates by Dr. J. McKenzie, of Loggieville.

Dr. A. F. Emery of Saint John, one of the senior members of the profession in New Brunswick has made a remarkable recovery from a serious abdominal operation. He is now up and about and is receiving the congratulations of his medical friends and old patients.

Several physicians in New Brunswick are planning to attend the meeting of the Canadian Medical Association in Victoria in June. A little booklet received this week from the Publicity Department in Victoria, contains information and photographs of conditions in that favoured part of the Dominion which makes the forthcoming trip appear more alluring, especially at this time of year when the Eastern Provinces are still firmly in the grasp of winter. A. STANLEY KIRKLAND

QUEBEC

GREAT DEMAND ON SANITARIUM

So great have been the applications for admission to the Ste. Agathe Tuberculosis Sanatorium that thirty additional beds have been added in the last few weeks. It has also been found necessary to convert some of the sitting rooms into temporary wards. Mr. L. S. Colwell, president of the association which took over the sanatorium from the Government last September, in company with Dr. J. Roddick Byers, recently inspected the institution. Dr. Byers stated that the capacity of the Sanatorium is now 239 beds with about 175 public patients being cared for. The problem of providing additional accommodation will have to be solved in the near future. A nurses' home is planned for this summer.

Hon. L. A. David, *Provincial Secretary*, in an interview announced his intention of submitting an amendment to Montreal's charter in the interest of public health to provide for the placarding of unsanitary dwellings. He explained that his proposal was to the effect that two warnings should be sent to the landlord of any dwelling which came under the eye of the civic health authorities, and that thereafter the house in question should be civically placarded as unsanitary. This would prevent its being rented, and would force the landlord, negligent hitherto, to do away with overcrowding, bad ventilation, insufficient plumbing and other causes of complaint.

The many friends of Dr. M. T. MacEachern will be interested in learning that this year he made a survey of the hospital system in Victoria, Australia at the request of the State Government. In the course of his survey, Dr. MacEachern found that that province was suffering from over-hospitalization. His recommendations to the Minister of Health include one on the need in the interests of economy and efficiency, of a considerable reduction in their number. Other recommendations are:—The need for

a fixed minimum standard of efficiency, to which private as well as public institutions must conform. He emphasized the need for a Hospital Bureau of Service and Information to collect up-to-date news of hospital methods and improvements and place it at the disposal of all hospitals in the province; also the desirability of creating a class of Intermediate Hospitals, or intermediate wards in the existing hospitals for the benefit of patients, who, while unable to pay full fees for private medical attention, do not come within the class of the sick poor. Contrasting hospital conditions in Melbourne with those in Montreal, Doctor MacEachern told a Melbourne newspaper:—"There are in this city 149 private hospitals, whereas in Montreal, a city of similar size, there are just eight or nine great general hospitals. The saving in money and energy is enormous."

McGill students have availed themselves freely of the health service provided for them through the Department of Physical Education, McGill University. From the beginning of the university year up to Feb. 9th, a total of 1,341 office consultations have been given, when necessary students are sent to hospital, and the health service takes care of the expenses of such students in the hospital for the first seven days. This free medical service has proved an important factor in protecting the health of the undergraduates.

We regret to record the continued illness of our esteemed Associate Medical Director, Dr. G. S. Mundie, of Montreal. Dr. Mundie has been ill for over a year, and is receiving treatment in the Royal Victoria Hospital. During his seven years of service with the Committee as Director of the Clinical Service in Montreal Dr. Mundie devoted himself whole-heartedly to the cause of mental hygiene, and has directed a large and arduous clinic. The sympathy of his many friends goes to Dr. Mundie in his long period of enforced absence from

the work to which he has rendered such notable leadership.

The organization of the department of child study and Nursery School, McGill University with Dr. A. B.

Chandler as Director is well under way. The Nursery School is located on the campus in a private residence which has been remodelled and redecorated. Suitable equipment has been procured, so that the building itself is now in running order.

GEORGE HALL

MANITOBA

Construction work will shortly be begun on a 100-bed addition to St. Joseph's Hospital, Salter St. and Pritchard Ave., Winnipeg. When the addition is completed the total capacity of the hospital will be 200 beds. The new building will run parallel to the old one, will be three storeys in height and will contain three operating rooms and a maternity department. The hospital is run by the Sisters of St. Joseph whose head house is in Toronto.

Dr. H. P. H. Galloway and Dr. Wm. Boyd left on March 20 for a western trip in connection with the extra-mural post-graduate scheme of the Canadian Medical Association. They will give addresses at Edmonton, Calgary, Vancouver and Victoria. Dr. Galloway will speak on Fractures and Dr. Boyd on Valvular Disease of the Heart.

The third Gordon Bell Memorial Lecture was given on April 1st, by Prof. Oskar Klotz, Toronto University, to a large and appreciative audience. His subject was "Aneurysm" a subject which on account of his re-

searches in arterial degeneration Dr. Klotz is particularly well qualified to discuss and it was treated in masterly fashion.

Dr. John Orr of Winnipeg has left for Saskatoon where he will take over his new duties in connection with the special survey of tuberculosis among Indians which is being carried out by the Anti-Tuberculosis League of Saskatchewan.

The fourth and last of the popular lectures arranged by the University of Manitoba was given on Feb. 26 by Dr. D. A. Stewart, Superintendent of the Manitoba Sanatorium and President of the Manitoba Medical Association, on "Disease, Its Influence on Human History."

Malcolm Byrd, secretary of the American Society of Psychical Research, addressed a number of Winnipeg medical men at the General Hospital on March 4 and at the Marlborough Hotel on the following day. His remarks were listened to with great interest and aroused considerable discussion.

ROSS MITCHELL

SASKATCHEWAN

A meeting of the Regina and District Medical Society was held on February 23rd, afternoon and evening, to receive the Canadian Medical Association post-graduate representatives. After luncheon at the General Hospital followed by a two-hour clinic at which over fifty members were present Dr. F. S. Patch of Montreal, and Dr. Duncan Graham of Toronto, both gave an excellent clinic covering ten cases. In the evening after a "moose dinner" in the Parliament Buildings, at which sixty-five members were present Dr. Graham gave a paper on rheumatic fever and Dr. Patch spoke on infections of the upper urinary tract. Both papers were much appreciated. After the addresses each lecturer answered a number of questions.

This was the first clinical event in the scheme of post-graduate medical education and it proved in every way a success.

Since our last annual meeting our local Society has listened to some good papers by local men. We try to have two for each monthly meeting. Some of these papers were as follows: Dr. Mitchell, "The environment of anaesthesia"; Dr. Alport, "The evolution and present status of gastric surgery"; Dr. Seig, "The difficulties in diagnosis of influenza"; Dr. McAllister, presented a case of cerebello-pontine tumour; Dr. Chase,

"The treatment of diabetes"; and Dr. Henry "A report of the International Radiological Convention in Cleveland."

Dr. J. E. Hanna, who formerly practised medicine at Madison, has opened an office at Ottawa.

Dr. M. A. McKinnon is now practising at Chamberlain. He was formerly at Wilcox, Sask.

Dr. B. McKinnon has moved his office from Margo to Invermay.

Dr. R. H. McCutcheon, who practised for many years at Humboldt, is now located in Vancouver. While in this province Dr. McCutcheon enjoyed a large and remunerative practise and his confreres regretted very much his departure.

Dr. McCartney has gone to Estevan, and associated himself with Dr. Creighton.

The General Hospital, Regina has secured Miss Irene Smith, as superintendent of nurses.

R. M. McALISTER

ALBERTA

Dr. Willis Merritt has returned home to Calgary from an enjoyable holiday in North Carolina.

Dr. A. M. Carlisle, who has spent several months in post graduate work at the Sick Children's Hospital,

Toronto, has returned to Wembley in the Peace River District.

Dr. C. B. Munroe, who formerly resided in Alberta, but for the past few years has resided in Los Angeles,

California, has now settled in the Arrowhead District, Southern Alberta.

The members of the Calgary Medical Society had the pleasure of listening to two instructive addresses on "Focal Infections" on February 2nd. Dr. J. W. Auld dealt especially with focal infections in the tonsils, nasal sinuses, kidney and prostate gland. J. W. Clay, D.D.S. ably discussed focal infections of the teeth and spoke at length on recent research work in this connection.

The executive committee of the Alberta Medical Association met in Edmonton on February 4, 1926, and decided to hold the annual meeting in this city during the second week in September. The exact date will be announced later. Four well known clinicians from Eastern Canada will take part in the programme, as well as Sir Henry Gauvain, widely known as a British authority on orthopaedic surgery. Every effort is being made to make this meeting a most successful one.

The Alberta Association for the Prevention of Tuberculosis is planning a "follow-up" to the recent survey with the idea of examining all those patients who have been treated in the Sanitarium and who have been discharged as cured or benefitted. The plan which has been suggested and which has been endorsed by the Alberta Medical Association is as follows, viz:—A physician from the Provincial Sanitarium, familiar with the records of discharged patients, from time to time should visit various parts of the province. Before doing so he would write to the different physicians in the locality, giving the names of their discharged sanitarium patients, asking that they be requested to appear in his office at a certain time, for examination and comparison of their condition with that on discharge from the sanitarium. The physician would be asked to have all contacts present for examination and any other cases he desired to refer to. The objects are mainly to discover cases of tuberculosis in the families of those already infected and to follow up and help if possible discharged sanitarium patients. A two year programme was suggested as a start, with the Provincial Anti-Tuberculosis Association paying the salary of the special physician and the Department of Health paying travelling expenses.

The annual meeting of the Council of the College of Physicians and Surgeons has been called for February 18th, in Edmonton, as the Provincial Legislature will be in session. It is expected that the Council will meet the members of the Government regarding the proposed legislation which would prevent physicians appealing to the Supreme Court against decisions of the Council. The court of last resort would be vested in the proposed Appeal Board of Laymen as referred to at length in the February number of the Journal.

Dr. E. A. Braithwaite of Edmonton has been appointed by the Provincial Department of Health to fill the newly created position of Inspector of Hospitals and Chief Coroner. He will review the case records where necessary and will have the power to order an investigation. Dr. Braithwaite is held in high regard by the medical profession in the Province in which he practised for over thirty years.

Dr. R. G. Brett, formerly Lieutenant-Governor of the province, is expected home from California shortly.

Dr. E. A. Bercov, of Edmonton, is relieving Dr. J. A. Tolmie of Coleman, who is taking a much needed holiday.

Dr. Walter Morrison of Smoky Lake has resigned as superintendent of the hospital, and will practice in Ontario.

Dr. J. E. Palmer of Calgary has returned from a holiday at the coast.

Dr. G. D. Stanley of Calgary, who has been spending the past month in California, returned home recently.

Dr. Stirling McGregor, who has just returned from post-graduate work in London, England, has accepted an appointment at the Brett Hospital in Banff.

At the annual meeting of the Council of the College of Physicians and Surgeons held in Edmonton, Dr. W. G. Anderson was elected president and Dr. W. T. Lamb of Camrose vice-president for 1926. Dr. George Johnson was re-appointed Registrar-Treasurer with Mr. W. G. Hunt as assistant.

The Council of the College of Physicians and Surgeons waited on the Provincial Government to protest against the proposed Bill for a Professions' Discipline Board composed of laymen, who would have the power to discipline members of the different professions, even to the erasure of the name, and their decision to be final and without appeal to the Courts. The Government promised due consideration of the arguments advanced.

At the meeting of the Calgary Medical Society held on March 2nd, the Rev. Dr. Robert Johnston addressed the members on the subject of "The Gift of Healing in the Christian Church." At the close of the discourse Drs. H. A. Gibson and R. E. Hughes opened the discussion in which a number of those present participated.

The Hoadley Professions' Discipline Bill was discussed at some length and the decision reached that a protest against this measure should be forwarded to the Government. This protest was subsequently drafted and sent forward.

A questionnaire has been submitted to the medical profession throughout the Province relative to the Hoadley proposal that the fees for maternity patients be reduced from the present rate to meet the requirements of poorer patients.

A large attendance is expected at the meetings to be held in Calgary and Edmonton, when Drs. Boyd and Galloway of Winnipeg will lecture on special pathological and orthopaedic subjects.

The town of Innisfail and district have endorsed the plan for a municipal hospital. Work will be commenced on the hospital building at an early date.

Under the grant to the Canadian Medical Association for extra-mural post-graduate courses, it has been decided to hold clinics the first week in July in the following places, viz:—Medicine Hat, Lethbridge, Calgary, Red Deer, Drumheller, Stettler, Camrose and Edmonton.

The by-law providing for a municipal hospital for the town of Vulcan and adjacent district was defeated when voted on recently. G. E. LEARMONTH

At the recent convention of the United Farm Women of Alberta, the Hon. George Hoadley, Minister of Health, stated that the present system of penalizing women a fee of twenty-five dollars in maternity cases was wrong in principle, especially in a country needing greater population. He believed that something should be done to relieve the mothers of financial

strain. What appeared to the women as a suggested bonus by the Government was received with loud applause. We are credibly informed that this was not the idea which the minister had in view, but rather that the physician's fee should be so adjusted

that a nominal charge of five or ten dollars should be made, and that other fees in general should be raised so that a living should be assured the physician whilst the mother would secure a reduction in fees at each accouchement.

G. E. LEARMONTH

BRITISH COLUMBIA

Dr. E. W. Ewart, who has recently been acting as assistant to Dr. H. B. Maxwell at Extension, Vancouver Island, has left for Orford Bay, B. C., to take charge of a contract practice.

The New Westminster profession has been rather unfortunate of late in that four of its practitioners have been laid up through sickness:— Dr. G. W. Sinclair, Dr. Bruce Cannon, Dr. G. T. Wilson and Dr. O. Van Etter. All are now quite recovered.

The March monthly meeting of the Fraser Valley Medical Society was held at New Westminster on March 4th, when Dr. G. E. Seldon, of Vancouver, gave a clinical address on: "Acute Abdominal Conditions."

The next regular meeting of the full executive of the B. C. Medical Association will be held on March 24th. This meeting has been planned to coincide with the visit of Dr. Wm. Boyd and Dr. H. P. H. Galloway of Winnipeg, who are coming out in connection with the extra-mural post-graduate educational scheme, of the Canadian Medical Association, and will speak on the evening of March 25th.

A luncheon meeting of the British Columbia Medical Association will be held on March 25th, at which Dr. Forrest Leeder, of Victoria, President-elect of the Canadian Medical Association, will speak on "Organization in Medicine." Dr. Leeder's capacities as a public speaker are well known, and we are sure that the knowledge that he is to speak will be a drawing card for all who have already heard him. We would again urge all members of that Association, throughout the Dominion, to make their arrangements with a view to taking in this meeting at Victoria, during the week commencing June 21st.

Dr. A. W. Hunter has resigned his position as Pathologist to the Vancouver General Hospital in order to devote more time to genito urinary work. Dr. Hunter still remains a member of the visiting staff of the Hospital.

Recent happenings in the Vancouver Police Court have brought forcibly to the attention of the medical profession certain changes that have been made in the

Narcotic and Drugs Act of Canada. Under this Act, as recently amended, it is unlawful for a medical man to prescribe any narcotic or drug to anyone who is an addict, whether the prescription be in writing or whether the drug be administered by the physician himself.

Dr. H. E. Young and Dr. Cyril Wace of Victoria visited Vancouver on March 2nd, and addressed the Vancouver Medical Association on behalf of the proposed solarium for crippled children, to be established shortly on Malahat Beach, Vancouver Island. The Women's Institute of this province has sponsored the movement and the solarium will be run under its auspices.

The March meeting of the Vancouver Medical Association was held in the University Club and was preceded by a dinner at which Drs. H. E. Young and Cyril Wace were the guests of the Association. After dinner the Annual Osler Lecture was delivered by Dr. E. D. Carder, his subject being "The Thymus." This paper was very much appreciated by all present.

The date for "Canadian Medical Night" of the Vancouver Medical Association has been fixed for March 25th. Dr. William Boyd and Dr. H. P. H. Galloway are to be the speakers of the evening. This meeting is the first to be held in Vancouver under the Extra-Mural Post-graduate Committee of the Dominion Association.

The Victoria Medical Society held its regular monthly meeting on March 1st, and the large attendance was unanimous in appreciation of the efforts of the Executive committee in providing such an excellent programme. Dr. Hermann M. Robertson of Victoria read a paper, on "A Case of Status Epilepticus (Traumatica) With Operation And recovery." This was discussed by Dr. Forrest Leeder and Dr. H. E. Ridewood.

Dr. H. Bundle Nelson, Radiologist at St. Joseph's Hospital, Victoria, read a paper on "High Blood Pressure, with a note on the Electrical Treatment." Discussion by Dr. W. M. Carr, Dr. Forrest Leeder and Dr. M. W. Thomas.

J. EVART CAMPBELL

UNITED STATES

The American Board of Otolaryngology has arranged for two examinations during the month of April as follows:—St. Paul's Sanitarium, Dallas, Texas, Monday, April 19th, at 9 a.m., Stanford University Medical

School, Clay and Webster Streets, San Francisco, California, Tuesday, April 27th, at 9 a.m. Applications may be secured from the Secretary, Dr. H. W. Loeb, 1402 South Grand Boulevard, St. Louis, Missouri.

Book Reviews

Light and Health. M. Luckiesh and A. J. Pacini. 302 pages, illustrated. Price \$5.00. Williams & Wilkins Co., Baltimore, 1926.

This book written by two laymen in clear, concise, correct English has much of interest for the physician. At the outset one is prejudiced by the title, which bears some resemblance to another well known book "Science and Health" the popularity of which is out of all proportion to its scientific merit. As one reads the various chapters this prejudice wanes and one is charmed by the many interesting statements made on the subject of "light". The writers show familiarity with the fundamental sciences of physics, biology and physiology. Scientific facts and the views of distinguished scientists are freely used to illustrate the subject matter and it may truly be said that the nature, value and indispensability of light to life is discussed in a learned manner. There is in most chapters a point where clear cut statements of scientific truth cease and therapeutic speculation begins. Light therapy is discussed in general terms but special emphasis is laid on ultraviolet radiation in which the writers are commercially interested. There is nothing intrinsically wrong in this form of enthusiasm but there arises in the mind of the well seasoned clinician a feeling that results are at times overrated. It is stated that ultra violet radiation benefits ulcer of stomach and intestines, mucus colitis, hay fever, bronchial asthma, pericardial effusion, many skin diseases including baldness, many infections including tuberculosis and pneumonia, high blood pressure and the vague group known as glandular or endocrine disturbances. One is amazed to find that obese people may be made thin and thin people made fat by the same radiations. It should be of special interest to some that re-juvenation is seriously considered. The quotation is as follows, "the use of ultraviolet radiations as a step toward re-juvenation has met with success" and "the general appearance becomes more youthful". The reviewer recognizes that light is a very valuable therapeutic agent and is quite as essential to life as air and water. He further admits that ultraviolet radiations have some place in therapeutics but he is not yet convinced that it will do what is claimed for it in this book. The book, however, has many points of merit and furnishes delightful reading and valuable information on a subject of great interest to physicians.

K. A. MACKENZIE

Abdominal Operations. Sir Berkeley Moynihan. Fourth edition, revised. 2 volumes, 1217 pages, illustrated. price \$22.00. W. B. Saunders Co., London and Philadelphia. McAinsh & Co., Toronto, 1926.

Sir Berkeley Moynihan has done in this great work the usual thing—for him; he has put himself into his book. The oft merited criticism in works on operative surgery of being a tedious, spiritless routine of "hows" and don'ts" has emphatically no application here. It comes to us fresh from his own operating theatre. While much descriptive and historical data are given of operations of many surgeons of great eminence, they are but parts in the background of the picture, and are brought into relief or dimmed according to the part the author would have them play in what is distinctly his own canvas. For Sir Berkeley tells of actual operations. You see him at work. You can almost scent the odor of the operating room, and visualize the "high Priest" and his "acolytes" in the "sacramental" surgical ritual so well described in chapter 2, volume 1. The author has to a high degree what Stevenson called the "knack of using words". His pictures become alive. Smoothness and literary

finish make bright and easy the numerous pathways of thought and action along which the student treads.

There is much more in this work than technique of operations. Pre-operative considerations have their rightful place. One gets the feeling, too, that when not to operate is perhaps more important than how to operate. From a vast experience the limits of diagnostic methods are well evolved, and a rational and definite place is fixed for the exploratory laparotomy. Every physical and psychical resource of the patient must be trained and coaxed into a pre-operative asset. If these are not sufficient, then recourse must be had to auxiliaries. Blood transfusion before and during operations are emphasized, and the technique described.

Post-operative considerations are no less elaborated. They are an essential part of the operation. The after treatment of gastro-enterostomy and the methods of meeting the various complications (chapter xii and xiii) may be quoted as illustrative of this outstanding element of the work.

Sir Berkeley rightly weaves into his structures the pathology of the living. Inferentially, one is convinced that no one knows pathology so well as the surgeon, because he sees it in action. All pre-operative diagnoses must bow to the realities revealed at operation. The various pathological lesions are well described and illustrated with cuts.

The student has the surgical anatomy of the abdomen presented to him in a markedly practical way. The classification of the lymph nodes in the field of operation is made to fit with the steps in the operation itself, and much anatomical confusion is avoided.

The work is made up in two volumes, divided into five sections and fifty-four chapters. Its workmanship and general appearance are excellent. The cuts are well executed, and there are not too many of them. The revision covers a period of ten years; and includes, therefore, what the Great War and the normal agents of progress have done for the science and craft of surgery. The whole work is practically rewritten.

Throughout, these are teaching books, in the best sense of this term; because the author has made good the dictum enunciated in chapter 2, that "in the craft of surgery the masterword is simplicity".

GEORGE H. MURPHY

Thoracic Surgery. Howard Lillenthal, M.D., F.A.C.S. In two volumes, with 904 illustrations, 13 in colors. 1273 pages. \$22.00. W. B. Saunders Company, London and Philadelphia. McAinsh & Co., Limited, Toronto, 1925.

Less than a generation ago, indeed up to the Great War, apart from the treatment of empyema, the thorax lay practically outside the sphere of surgery. In America this was especially the case. Now two volumes of nearly thirteen hundred pages, can be written about chest surgery, and even then the impression is given of terseness and exactness of statement rather than of over-elaboration. The author aims to "give to the general medical profession a guide to the diagnosis of surgical thoracic diseases", and the possibilities of their help through operation. To the surgeon he offers the results of his own wide experience, rounded out by references to the teachings of others. It is significant of the new era that among diseases which may now be helped by chest surgery is pulmonary tuberculosis, to which in one way or another a fourth or fifth of the book is devoted; and even also mitral stenosis. Amberson and Peters contribute 120 pages on artificial pneumothorax which Lillenthal considers (and we cordially agree) that surgeons should know more about than

they do, since what it can and cannot accomplish makes the indications or contra-indications for the more drastic surgical measures, the removal of ribs to collapse the chest wall upon a diseased lung, or phrenectomy to raise a hemi-diaphragm. The new surgery which invades even the heart ventricle to slit a hardened mitral valve is just another illustration of the invasion of the thorax, and of the treatment of "medical" diseases, by the surgeon.

The wide range and ample discussion of the subject in this work may be appreciated from the giving of sixty pages to the mediastinum, and most usefully, ninety-one to the esophagus with 74 illustrations, 125 to the pericardium, heart and great vessels, 41 to the chest wall, 48 to the diaphragm, 108 pages with 71 illustrations to empyema, acute and chronic, and no fewer than 194 pages, with 211 illustrations to bronchiectasis and abscess. Dr. Evarts A. Graham, himself a chest surgeon of distinction, and originator of lobectomy by cautery, contributes a chapter on the physiology of the respiratory tract, Yankauer writes on bronchoscopy and endoscopy generally, Branower on general anaesthesia, Ottenberg on blood transfusion and Leopold Jaeches contributes 55 pages on roentgenology. The fact that in this section on roentgenology all the references are German may explain the wide divergence of the writer's views from those universally accepted in America as to the necessity of stereoscopic films for chest diagnosis, the great value of intensifying screens, and the obsolescence of the gas tube. It may explain also why his standards of classification of tuberculous lesions are quite different from official standards in the United States and Canada. Such differences in a book for use chiefly in these countries tend only to confusion. Apart from these defects there is much in the section that is of value.

The many and excellent illustrations—nearly one thousand, with thirteen in colour—strengthen the impression that neither pains nor cost have been spared to make this a monumental work. Besides the familiar plates showing dissections and operations a liberal use has been made of radiographs, and also of diagrammatic drawings. The relations of the chest structures are rendered clear by nine full-page annotated illustrations of as many cross sections at different chest levels.

Dr. Lillenthal is happy in the birth-time of his big book, coming at the end of a decade of revolutionary chest surgery, and at a time when wider use of the newer methods is called for. We can scarcely imagine a practitioner of medicine whatever his bent, who would not find much that is of interest in it. It should be in the library of every general surgeon. And it will find a special use in the hands of general surgeons whose special experience and equipment lead toward thoracic surgery, and who may wish to conquer this newer hemisphere of their science and art.

D. A. STEWART

Our Present Knowledge of Heredity. A series of lectures given at the Mayo Foundation and elsewhere during the years 1923-24. 250 pages, illustrated. Price \$2.50. London and Philadelphia, W. B. Saunders Co.; Toronto: McInsh & Co.

This small book (250 pages) comprises a series of six lectures delivered by well known authorities, each of whom has increased the knowledge of heredity and kindred problems by original research. It is therefore admirably suited not only to those who have worked along these particular lines, but to the very widely distributed public who are interested in these problems. The facts and deductions are presented with a clearness and sanity which makes this book an exceedingly readable one.

The lecture by W. E. Castle deals with the general problem and historical setting. He takes up the relation of the chromosomes to heredity, Mendel's law, sex linked characters and other points in an exceedingly clear outline. Excellent photographic illustrations add

to the value of the account. The second lecture by C. E. McClung treats of the subject of the heredity of sex. The inheritance of acquired characters is considered in the third lecture by J. A. Detlefsen. An outline of the views of Darwin, Lamarck and Weismann is given and an account of some of the very interesting research done in this connection. A bibliography accompanies this lecture. In "heredity in relation to cancer" Maud Slye sets out her views simply and clearly. An account of the long series of careful experiments with mice developing spontaneous tumours is given. It is pointed out how, with a carefully analyzed strain of animals, the unit characters recur following the Mendelian expectation. Her objections against the statistical method of studying the inheritability of cancer in man are stated with force. Many charts illustrating the results are given. The influence of heredity on the occurrence of cancer is discussed fully by H. Gideon Wells. The question of cancer families in man is dealt with, and the striking evidence obtained from the transplantation and spontaneous incidence of tumours in animals is fully canvassed. A bibliography is given. The lecture on eugenics by M. F. Guyer calls attention to the serious nature of the race problems which are facing society, quoting the statistics of mental diseases and criminalism, the contamination of good strains and the birth rates in normals and defectives. The question of mental deficiency and crime incidence among foreign born immigrants is investigated. His arguments and inferences are stated lucidly and with energy, and his setting out of these serious problems should be of interest to any public spirited woman or man. V. H. R. MOORHOUSE

Manipulative Surgery. A. G. Timbrell Fisher, M.C., F.R.C.S., 168 pages, 62 illustrations. Price 7/6 net. H. K. Lewis & Co., 28 Gower St., London, W. C. I. 1925.

The object of this book is "to again draw the attention of the medical profession to the great importance and value of manipulative surgery in the treatment, in carefully selected cases, of certain of the sequelae of injuries and diseases particularly affecting joints, muscles, tendons and fascia."

This, the author has done, clearly, concisely, and adequately. He recognizes what is good in the bone-setter and his practice, and while setting forth the causes of failure, he makes it obvious that such cases should be treated by the regular practitioner according to scientific principles and proper methods.

The author gives the pathology of cases that "bone-setters" cure and points out the dangers of misapplied manipulations. The chapters on general principles are good, and fulfill the requirements.

Completeness is given to the work in the chapters on treatment according to the regions affected; notes on the after treatment; and helpful illustrations.

The author has dealt with the case of the bone-setter in a broadminded way, and the profession will be well repaid in noting carefully what he says about this side of the problem, as well as the problem itself and the employment of manipulative methods in dealing with it.

It is a satisfying little book and should be known to every practitioner. J. G. MACDOUGALL

Pseudo-Appendicitis. A study of Mechanical Syndromes of the Right Lower Quadrant Simulating Appendicitis. By Thierry de Martel and Edouard Antoine. Translated by James A. Evans, A.B., M.D. 211 pages, 41 engravings. Price \$3.00 net. F. A. Davis Co., Philadelphia, 1925.

This is another work calling for more careful examination of cases presenting the "right iliac syndrome." The authors in this small book of 201 pages deal with those conditions which may give rise to pain and tenderness in the right lower quadrant of the ab-

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domen. The symptomatology, physical findings and radiological findings of each condition are given. Case reports are presented illustrating each type of case. The chapter on diagnosis is especially good. The treatment recommended—medical and surgical, with the indications for the use of each—is sound.

This book should be of interest to internists, radiologists and surgeons as the co-operation of these is necessary in the care of these cases. A. B. SCHINBEIN

Submucous Endocapsular Tonsil Enucleations. Charles Conrad Miller, M.D. 218 pages. The Oak Printing & Publishing Co., Chicago, 1925.

This little book of 218 pages, commences with an interesting review of the evolution of tonsil surgery. The author says that now tonsillectomy is generally regarded as the operation of choice. He thinks, however, that the method usually employed has numerous drawbacks, and has devised a new form of operation. He incises the mucous membrane of the tonsil and strips it back. He then removes the glandular tissue by dissection or by the tonsil punch, leaving the capsule intact. He considers this operation an improvement on tonsillectomy, for numerous reasons, amongst them being less hemorrhage, earlier healing, less post-operative infections and less scarring of the soft palate and pharyngeal wall.

There are numerous diagrams in the book; but comparatively little data concerning the operation. The author then gives a somewhat superficial outline of post-operative technique including transfusion for hemorrhage, and of tonsillar infections.

The book is called "Excerpts from Clinics" given by the author and is interesting in giving his viewpoint on the treatment of throat and tonsillar infections.

G. E. HODGE

Practical Pharmacognosy. T. E. Wallis, B.Sc., F.I.C., Ph.C. With a Foreword by H. G. Greenish, D.S. Sc., F.I.C., F.L.S. 115 pages, 81 illustrations. Price 7/6. J. & A. Churchill, 7 Great Marlborough St., London; The Macmillan Co. of Canada, Toronto, 1925.

This is a valuable little book, extremely well illustrated, and giving lessons in pharmacognosy which would give a student of pharmacy ample introductory knowledge to the practical application of this subject. Unfortunately, it furnishes an excellent example of the lack of contact between modern medicine and schools of pharmacy as it contains almost no hints as to the study of powdered drugs, which is the form in which the pharmacist most frequently purchases the same if he does use crude drugs. A great many of the examples are from plants which no longer are frequently employed in medicine. The whole subject of pharmacognosy wants to be taken up by men who have realized that Meze-reon, Chamomile and Bryonia and others that might be mentioned, are no longer of much importance from a medical standpoint. V. E. HENDERSON

Favourite Prescriptions. Espine Ward, M.D. 92 pages. Price 5/-. J. & A. Churchill, 7 Great Marlborough St., London; The Macmillan Co. of Canada, Toronto, 1926.

This little compendium contains as its motto, "For many patients hope is the best medicine," and certainly a careful examination of some of the prescriptions would lead one to consider that quite possibly it would contribute more to the cure and alleviation of the patient than the medicine itself. As typical examples might be taken some of the cough mixtures. For example, one which must be particularly disagreeable contains tincture and infusion of senega, ammonium carbonate and the compound tincture of camphor, for a patient with loose sputum. Surely if the sputum is loose, by which I think most persons would understand

not viscous, then the cilia of the bronchial tree should be able to handle it, and if not, cough is necessary to clear the tubes. Yet we have two ingredients or three to increase the production of secretion and one to decrease the cough. Further we find tincture of digitalis combined with the spirits of nitrous ether, the acetate of squills, potassium acetate, and the infusion of scoparium; a shotgun mixture of an antique type recommended for dropsy, where the digitalis would be made largely inert by the acidity of the mixture in a very short time.

These examples are sufficient to show the nature of the book. I have no doubt that some of the prescriptions are useful if used intelligently, but there is little indication as to types of condition for which each may be used and many of them are old fashioned in the extreme. The hints on poisoning are, as the author acknowledges, an abbreviation of Murrell and can by no means replace this book in the physician's emergency bag. V. E. HENDERSON

Mental Invalids. C. C. Easterbrook, M.A., M.D., F.R.C.P.E. 86 pages. Price 5/- net. Oliver & Boyd, Tweeddale Court, Edinburgh, 1925.

This slim volume of some eighty pages contains the Morison lectures delivered before the Royal College of Physicians of Edinburgh in June, 1925.

In his foreword the author states his purpose to discuss some practical problems that have engaged his attention during thirty years of psychiatric experience. His aim throughout this experience has been to establish facts, to consider their meaning and to deduce from them principles of practice.

It is evident throughout that he has kept himself well abreast of the voluminous literature that has appeared in the psychiatric field in the past few years. To a careful culling of this great mass he has added the leaven of his own ample experience and the result is a fairly concise, well arranged statement of present day psychiatric doctrine.

The first chapter under the caption "The Body Mind" is taken up with an exposition of integration in the individual and could be read with profit by all medical men since it states clearly one outstanding particular in which present day psychiatric thought and practice is both more scientific and more human than that of general medicine, viz., the consideration of the whole individual patient, body, and mind, a thing of many parts so closely knit together in structure and function, so dependent the one on the other, that attempted separate consideration is bound to result in an artificial and incomplete survey. This is a lesson that those who work in the field of mental medicine have learned, and it is one that a great many men who work in the wider fields of medicine must learn and are learning.

The second and fourth chapters on the "Clinical Examination of Mental Invalids" and the "Classification of Mental Diseases" contain little that is new. The ideas expressed are sound and acceptable but clinical examination methods are most often a matter of individual preference; the desired end, the accumulation of accurate facts concerning the individual patient's life and the correct interpretation of them may be attained in a variety of equally valuable ways. Classification is in a state of considerable unrest just now and one feels thankful this is so. The adoption of a stereotyped classification of mental disease almost certainly means stasis of thought and the too early abandonment of the major problem—the interpretation of an ever changing picture.

The third chapter on causation is a well rounded out statement of what is known about the etiology of mental disease. The author includes a valuable table of different forms of stress or exciting factors.

In the final chapter, the author deals with treatment. He stresses the need for early care and pleads

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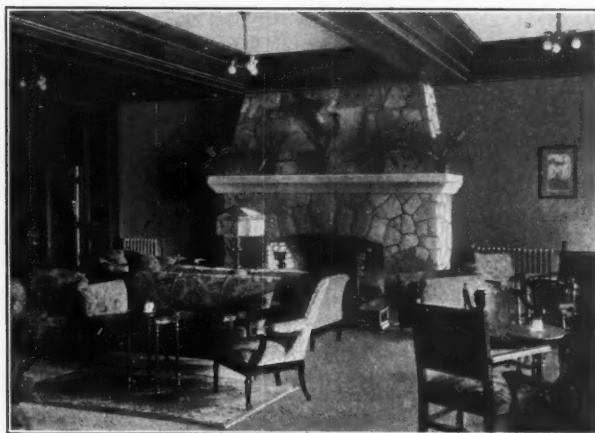
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for an extension of the voluntary admission privilege. It is plain that in this respect the Old Country lags behind many communities in this country and the United States. Other points touched upon are the value of occupational therapy, psychotherapy and open air rest treatment.

Taken as a whole the book is well worth reading. Its subject matter is thought provoking and standing as it does close to the forefront of orthodox teaching may be accepted as a short, logically arranged statement of psychiatric faith embellished throughout by ripe scholarship and broad experience.

A. T. MATHERS

Collected Papers of the Mayo Clinic and the Mayo Foundation. Edited by Mrs. M. H. Mellish. Vol. XVI, 1924. 1331 pages, 254 illustrations. Price \$13.00. W. B. Saunders Co., London and Philadelphia. McAlinsh & Co., Toronto.

This book is a record of all papers for the year 1924 from the Mayo Clinic and Mayo Foundation. On account of the mass of material covered it has been necessary to abridge or abstract many of the papers, while others are merely referred to by their title. As such, the work is of value chiefly for reference as to the important advances in the various branches of medicine and surgery during the year. It is felt that the last sixty pages might better have been employed in the publication of more of these valuable papers in full, than in their present use of the printing of a series of addresses and reports of little interest except to those members of the associations before whom they were delivered.

L. H. MCKIM

Rational Gland Therapy for Women. I. Wanless Dickson, M.B., F.R.C.S. 96 pages. Price 4/6 net. The H. K. Lewis Co., 28 Gower St., London, W.C.1, 1926.

In this thesis, the author presents the various menstrual phenomena, both physiological and pathological, on an endocrinological basis. He first shows, that, not only normal menstruation, but also dysmenorrhoea in its various forms, menorrhagia and metrorrhagia, the menopause, vomiting of pregnancy etc., are all dependent on endocrine activity. With this as a basis, extracts of various glands are administered to correct the disturbance. His conclusions are based on many years of study of actual cases.

No stereotyped form of treatment can be laid down for any case, but, since mammary substance inhibits ovarian action, it is useful in cases of congestive dysmenorrhoea, in menorrhagias and metrorrhagias. Ovarian extract is especially useful in combating the malaise and headache of the menopause; corpus luteum for the hyperpiesis of the menopause, and mammary substance if hemorrhages are troublesome.

The book is concise and clearly written; the cases cited add a great deal to making clear the rationale of the treatment given. Although the author states that "endocrines are not a panacea for all ills" one feels that he is an enthusiast on the subject, and that results obtained from glandular therapy are not always as glowing as are depicted.

ELEANOR PERCIVAL

Lead Poisoning. Joseph C. Aub, Lawrence T. Fairhall, A. S. Minot and Paul Reznikoff. Vol. vii, in four parts. 256 pages, 35 illustrations. Price \$4.00. The Williams & Wilkins Co., Baltimore, 1926.

The monograph is becoming one of the most convenient methods for presenting subjects compactly and yet with reasonable completeness. It occupies a halfway position between the journal and the textbook, and rather careful handling is required to keep it within this middle course, the greater difficulty perhaps being to keep it from becoming of too great a compass. It must not be thought, however, that a series of monographs will substitute the textbook any

more than would a series of papers, nor are they expected to by the authors of the series under consideration. They are designed, we are told, as "critical digests in convenient and readable form"; as "comprehensive reviews". Such qualities are by no means easily ensured in these days of multitudinous journals, but if this volume is a fair sample of the series, one may grant that success has been attained. We read that the literature on lead poisoning has not been fully covered by this monograph, and yet the authors' files contain over 2,200 references. This should provide a very solid groundwork.

The subject has been admirably analyzed in its various aspects, and although some of the more technical laboratory details will be valuable chiefly to the laboratory worker, still the physician in general practice, as well as the man interested in industrial medicine, and even the teacher of clinical medicine may all find material of practical value and great interest in many of the chapters. Modern views on the absorption of lead, its effects on the blood cells and on the germ cells, the diagnosis and treatment of symptoms, and the prevalence of industrial poisoning are well presented.

It is hardly necessary to dwell on the ubiquitous occurrence of lead, not only in industry but also in such vital and unexpected quarters as water supplies, cosmetics, drugs and home-made beverages. This monograph will serve as a well-balanced and timely review of the whole subject.

H. E. MACDERMOT

The Diseases of Children. Sir James Frederic Goodhart, Bart., M.D., LL.D., Aberd., F.R.C.P. 966 pages, 66 illustrations. Price \$8.50. Lea & Febiger, S. Washington Square, Philadelphia, 1926.

This is the twelfth edition of a book that was originally published some forty years ago by the late Sir James Goodhart. It has been again revised and enlarged by Dr. F. G. Still of London, who claims to have retained untouched much of the original work. At the same time he has endeavored to incorporate the important advances that have been made during the past five years since the 11th edition appeared. New chapters have been added on such subjects as erythredema, (acrodymia) and encephalitis lethargica, while many of the newer discoveries like insulin and the vitamins have been given their place. The history of the book explains the reason for many of the references dating back to the early "eighties".

The book is remarkably complete for so small a volume. This has been made possible by the omission of all pathological chemistry and clinical pathology—although the morbid anatomy is well described. Many of the rarer disorders of childhood (such as cirrhosis of the liver and cleido-cranial dysostosis) are briefly mentioned.

One cannot help being struck by the faith that is placed in medicinal remedies, many of which might be considered in the nature of placebos. The treatment of scarlatina seems to be unnecessarily detailed and somewhat antiquated. Much space is devoted to an account of a number of antiseptic emollients for anointing the skin. Many drugs are recommended for the "scarlatinal drowsy", as well as for the sore throat. Carbolic acid should be freely sprinkled about the room and the latter afterwards fumigated by burning sulphur.

Hamorrhagic disease of the newborn is not given the emphasis one would consider it deserved. Nor is the specific action of human blood in the treatment of this disorder sufficiently emphasized, for it is placed in the same category as gelatine, calcium chloride and adrenalin, as one of the many things that may be used. It is difficult to appraise the chapters dealing with infant feeding, as English views and methods are different from those on this side of the Atlantic. Artificial formulae are advised to conform as nearly

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as possible to the composition of breast milk; 4 per cent fat being considered essential. Most of the difficulties met with in artificial feeding are referred to the indigestibility of the curd which must be reduced to a minimum or modified by the addition of an alkali or by peptonization. For a marantic infant a cream and barley water mixture containing almost no curd is advised. The prevalent use of canned infant foods in England calls for careful consideration of the use and abuse of such methods of feeding.

Taken as a whole the book will be found a useful one for practitioners, who will find a graphic description of diseases and disorders of childhood depicted in the delightful style which is characteristic of Dr. Still. It is well printed and is of a convenient size.

L. M. LINDSAY

Lectures on Nutrition. A series of lectures given at the Mayo Foundation and elsewhere during the years 1924-25. 243 pages, illustrated. Price \$2.50. London and Philadelphia, W. B. Saunders Co.; Toronto, McAllister & Co.

This is the second volume of a series which is, in these days of tremendously rapid output of new research, of a type becoming absolutely essential not only for the educated public who wish to keep in touch with modern advances in science, but also for the physician who wishes to know and apply the latest advances of related sciences, and even for the research specialist, if he wishes to keep up to date in branches of work other than the narrow outlook of his own specialty.

The idea underlying the course of lectures now published is admirable. Authorities on particular problems of nutrition, who have become authorities by reason of the advances they have themselves made, have, each dealing with their own problems, linked together in ordered sequence so much of the subject that, while no claim is made for complete treatment "the volume is a statement by competent authorities of our present-day knowledge of most of the important problems of nutrition".

Dr. F. G. Benedict, in dealing with "The measurement and significance of basal metabolism" gives an account of many of the actual experiments which have defined the necessary precautions to be observed in making a basal metabolism test. Thus he has shown that a slight movement of the hand even once a minute has a negligible effect, but that one movement of the leg per minute definitely vitiates a result, so that leg movements must be proscribed. The use of a small, non-stimulating breakfast, a prone or reclining posture, the necessary surrounding temperature, etc., are all dealt with. The potentialities of basal metabolism rate measurements, as visualized by the master of the subject, are worth quoting in full: "Modern, simplified methods make possible the determination of basal metabolism with a technique that is much easier than the technique for counting the blood corpuscles, and with an instrument that is not appreciably more expensive. In fact, it is not perhaps too speculative to state that the present wave of enthusiasm for basal metabolism measurements and their application primarily to endocrine disturbances may in time be replaced by more rational use of this important measurement as an index of general vigor, tone, and physiologic state."

Graham Lusk in "Problems of Metabolism" deals with such points as the still controversial relation of heat production to surface area, the effect of proteins and protein derivatives on heat production, and the metabolism of fats and carbohydrates.

E. F. DuBois deals with "The proportions in which protein, fat, and carbohydrate are metabolized in disease", illustrating the data by a simple graphical method. He emphasizes the fact that the condition of undernutrition has not received sufficient attention in metabolism measurements.

A. V. Hill discusses "Muscular activity and carbohydrate metabolism" and deduces definitely that no matter what the diet, in health or disease, the primary fuel of muscle is carbohydrate; the essential element in the machinery is lactic acid, itself derived from carbohydrate; other food material (fat, protein) must therefore be transformed to carbohydrate for the purpose of muscular activity.

E. V. McCollum deals fully with five vitamins (some writers now claim six) both from the chemical and pathological standpoints. Not the least interesting of his remarks is the association of a description by David Livingstone in 1857 of a peculiar eye condition amongst members of his exploration party whilst on deficient diet with the ophthalmia now associated with lack of vitamin A. Far greater pathological changes appear to be associated with deficiency of this vitamin than is generally known. Since a fairly complete account of "biostearin", claimed by Takahashi to be pure vitamin A, is included, it should be mentioned that in the December number of the *Biochemical Journal* Professor J. C. Drummond has dealt a very damaging blow to this claim, advancing strong evidence that "biostearin" is a mixture, including even some toxic material. Apparently we are still some distance from the isolation of any of these important chemical compounds in a pure condition.

Finally Evans on "The relation between fertility and nutrition" gives a full account of his work on fat-soluble vitamin E, associated with reproduction.

Obviously, the book should be in the hands of every physician. Its low price need not be considered to detract from its value.

A. T. CAMERON

Puerperal Septicæmia: Its Causation, Symptoms, Prevention and Treatment. George Geddes, M.D., C.M. 200 pages with charts. Price \$3.75. John Wright & Sons, Ltd., Bristol. The Macmillan Co., of Canada, St. Martin's House, Toronto, 1926.

This book is very well written and is well worth reading by both the medical practitioner and the specialist.

The author sets out to prove that the incidence of puerperal infection has something to do with industrial accidents, and it must be acknowledged that he does seem to prove this point. His statistics may be quite true for some industrial centres in Great Britain, but we do not think that the connection between industrial accidents and puerperal infection will hold true for many sections of Canada.

He has great courage in putting the blame of puerperal sepsis on the medical practitioner, and his statistics prove that the midwife is not the important factor in the etiology of puerperal sepsis. His recommendation that the practitioner should exercise more care than usual after dressing wounds is good, and the routine wearing of rubber gloves will undoubtedly help to improve the statistics.

Few in Canada will agree with the author's enthusiasm for curetting the uterus in cases of puerperal sepsis.

L. C. CONN

Food for the Diabetic. Mary Pascoe Huddleson. Introduction by Nellis Barnes Foster, M.D. 83 pages. Price \$1.40. The Macmillan Co., of Canada, Toronto, 1926.

In this little book the sufferer from diabetes will find safe rules to follow in order to ensure his well-being. Dealing chiefly with dietary, it teaches one how to calculate caloric values and weigh food by means of the common household measures, and supplies appropriate menus and recipes.

The second edition explains the principles of insulin therapy with the same commendable avoidance of technical language. Concise, up-to-date, and easily readable, it can be recommended both to the diabetic and the practising physician as a useful guide.

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Chronic Infection of the Jaws. Stanley Colyer, M.D., M.R.C.P. 75 pages, 36 illustrations on 19 plates. Price 18/6 net. H. K. Lewis & Co., 28 Gower St., London, W.C.I., 1926.

Dr. Colyer has brought before the medical and dental profession a very much needed article, one that should be carefully read by every active man in the profession.

With the radiograms of the teeth he has worked out the details and has shown how an apparently innocent gingivitis may cause the graver organic changes so often found and hard to explain.

The author's idea of dividing patients into two classes, sclerosing or gouty type and non-sclerosing or arthritic type, is good, because it gives the diagnostician a basis on which to work.

His conception of the importance of interpretation of radiograms is well taken, as so very much depends upon this. On the cause of failures in many cases his citation of "incorrect diagnosis" stands out, for certainly a class of disease that is undermining the health of such a great proportion of the population should bear the closest study and investigation. This can be determined only by correct knowledge of the causes, and Dr. Colyer in his book has done excellent work in giving us this knowledge in a clear and concise manner.

The chapters in rheumatoid-arthritis, anæmia, pyrexia of unknown origin, eye and skin diseases, arterial tension and heart diseases require no comment, other than the fact that he has shown a much closer relationship than has so far been acknowledged between these diseases and jaw infections.

GEO. E. SELDON

Heliotherapy at Low Altitudes.—The use of the principles of heliotherapy as laid down by Rollier has become well nigh universal. This would seem to be an acknowledgement that it is possible to offer patients the advantages of heliotherapy far away from an environment like that of Rollier's Alpine sanatorium. Albert H. Freiberg, Cincinnati, points out that some of the most enthusiastic advocacy of Rollier's methods comes from men who are working in situations as different from his as can well be imagined. Such as Gauvin in England, Kisch in Germany, Lo Grasso of Perrysburg, N. Y., and Hyde of Akron, Ohio. All of them are agreed that it is possible to do the same things for surgical tuberculosis in low altitudes as Rollier is able to do in the Alpine highland. Kisch asserts that, in the institution at Hohenlychen near Berlin, it is possible for him to attain cures as rapidly as is the case at Leysin, and that his statement is made with a thorough familiarity with the situation here by reason of several weeks' residence for study. He holds that there is a distinct advantage in having the tuberculous patient cured in the very same environment in which his disease was acquired and that it may be assumed possible, in this way, to avoid many of the recurrences that are otherwise to be expected. Kisch has found it possible to accomplish results in every way comparable to those obtained at Leysin in the neighbourhood of Berlin, at an altitude approximating that of sea level. He believes that the most important element of the solar light, in its therapeutic aspect, is to be found in the heat rays: the red and infra-red portion of the spectrum. He believes that their activity

stands in direct relationship to the surface temperature produced, and that this must approximate that which is produced by the sun itself. He requires, on this account, surface temperatures varying between 107 and 117 F. (from 42 to 47 C.). These he produces by means of lamps that are especially rich in heat rays; the electric current or the oxyacetylene blast are the means of their activation. He maintains the possibility of producing by this means pigmentation which is comparable to that resulting from insolation both in hue and in intensity. Freiberg discusses at length the application of heliotherapy in tuberculous conditions of the joints and pleads for the application of all forms of treatment as the individual case may require. He says: Heliotherapy is a marvelous addition to our resources, but it works no miracles; it brings to our aid no biologic resources of unprecedented character; it produces no new cartilage in place of that which has been utterly destroyed; it makes the processes of cicatrization no less necessary than they have been hitherto. At the same time, by its benevolent action cicatrization is made more sure and more rapid. When destruction of four or five vertebral bodies and the consequent collapse have brought about a gibbous deformity, we may hope to bring about fusion of the contacting, diseased surfaces more rapidly and more surely than used to be possible without heliotherapy at our disposal. By postural methods we are enabled to improve greatly the appearance and even the function of the spine through corrections above and below the actual seat of disease.—*Jour. Am. Med. Ass.*, March 13, 1926